Answer 1:

Bibliographic Information

Mouse mammary tumor virus promoter-containing retroviral promoter conversion vectors for gene-directed enzyme prodrug therapy are functional in vitro and in vivo. Klein, Reinhard; Ruttkowski, Baerbel; Schwab, Sonja; Peterbauer, Thomas; Salmons, Brian; Guenzburg, Walter H.; Hohenadl, Christine. Austrianova Biotechnology GmbH, Vienna, Austria. Journal of Biomedicine and Biotechnology (2008), No pp. given. Publisher: Hindawi Publishing Corp., CODEN: JBBOAJ ISSN: 1110-7251. http://www.hindawi.com/GetArticle.aspx?doi=10.1155/2008/683505 Journal; Online Computer File written in English. CAN 149:167378 AN 2008:782531 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Gene directed-enzyme prodrug therapy (GDEPT) is an approach for sensitization of tumor cells to an enzymically activated, otherwise nontoxic, prodrug. Cytochrome P 450 2B1 (CYP2B1) metabolizes the prodrugs cyclophosphamide (CPA) and ifosfamide (IFA) to produce the cytotoxic substances phosphoramide mustard and isophosphoramide mustard as well as the byproduct acrolein. We have constructed a retroviral promoter conversion (ProCon) vector for breast cancer GDEPT. The vector allows expression of CYP2B1 from the mouse mammary tumor virus (MMTV) promoter known to be active in the mammary glands of transgenic animals. It is anticipated to be used for the generation of encapsulated viral vector producing cells which, when placed inside or close to a tumor, will act as suppliers of the therapeutic CYP2B1 protein as well as of the therapeutic vector itself. The generated vector was effectively packaged by virus producing cells and allowed the prodn. of high levels of enzymically active CYP2B1 in infected cells which sensitized them to killing upon treatment with both IFA and CPA. Detn. of the resp. IC50 values demonstrated that the effective IFA dose was reduced by sixteen folds. Infection efficiencies in vivo were detd. using a reporter gene-bearing vector in a mammary cancer cell-derived xenograft tumor mouse model.

Answer 2:

Bibliographic Information

Low-dose metronomic cyclophosphamide treatment mediates ischemia-dependent K-ras mutation in colorectal carcinoma xenografts. Shahrzad, S.; Shirasawa, S.; Sasazuki, T.; Rak, J. W.; Coomber, B. L. Department of Biomedical Sciences, University of Guelph, Guelph, ON, Can. Oncogene (2008), 27(26), 3729-3738. Publisher: Nature Publishing Group, CODEN: ONCNES ISSN: 0950-9232. Journal written in English. AN 2008:704510 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Antiangiogenic therapies are promising approaches to cancer control, but the details of their effects on subsequent tumor progression are not fully understood. Such therapies have the potential to eventually generate extensive amts. of tumor ischemia, and we previously demonstrated that ischemic conditions induce K-ras mutations in cells with deficient mismatch repair (MMR) mechanisms. This suggested that similar effects on oncogene mutagenesis may accompany antiangiogenic therapy. To test this, MMR-deficient colorectal cancer cells (Dks-8) were xenografted into immune-deficient mice and treated with the antiangiogenic regimen of low-dose/metronomic cyclophosphamide for 2 wk followed by a 2-wk recovery period without therapy. This treatment resulted in transient tumor growth inhibition, increased hypoxia, and decreased microvessel d., and cancer cells from treated tumors acquired activating mutations of the K-ras oncogene (K-rasG13D). In vitro exposure of Dks-8 cells to the active metabolite of cyclophosphamide (4-hydroxycyclophosphamide) had no effect on the K-ras status, indicating that there was no direct action of this alkylating agent on K-ras mutagenesis. In addn., cells sorted from hypoxic regions of Dks-8 tumors were enriched in K-rasG13D mutants. Collectively, our studies suggest that increases in tumor hypoxia induced by antiangiogenic treatment may lead to K-ras mutation and consequently tumor progression, esp. in susceptible individuals.

Answer 3:

Bibliographic Information

Biodistribution and predictive value of 18F-fluorocyclophosphamide in mice bearing human breast cancer xenografts. Kesner, Amanda L.; Hsueh, Wei-Ann; Htet, Nwe Linn; Pio, Betty S.; Czernin, Johannes; Pegram, Mark D.; Phelps, Michael E.; Silverman, Daniel H. S. Ahmanson Biological Imaging Division, Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA. Journal of Nuclear Medicine (2007), 48(12), 2021-2027. Publisher: Society of Nuclear Medicine, CODEN: JNMEAQ ISSN: 0161-5505. Journal written in English. CAN 148:420313 AN 2008:79050 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In mice bearing human breast cancer xenografts, we examd. the biodistribution of 18F-fluorocyclophosphamide (18F-F-CP) to evaluate its potential as a noninvasive prognostic tool for predicting the resistance of tumors to cyclophosphamide therapy. Methods: 18F-F-CP was synthesized as we recently described, and PET data were acquired after administration of 18F-F-CP in mice bearing human breast cancer xenografts (MCF-7 cells). Tracer biodistribution in reconstructed images was quantified by region-of-interest anal. Distribution was also assessed by harvesting dissected organs, tumors, and blood, detg. 18F content in each tissue with a γ-well counter. The mice were subsequently treated with cyclophosphamide, and tumor size was monitored for at least 3 wk after chemotherapy administration. Results: The distribution of harvested activity correlated strongly with distribution obsd. in PET images. Target organs were related to routes of metab. and excretion. 18F-F-CP uptake was highest in kidneys, lowest in brain, and intermediate in tumors, as detd. by both image-based and tissue-based measurements. 18F-F-CP uptake was not inhibited by coadministration of an approx. $\times$700 concn. of unlabeled cyclophosphamide. PET measures of 18F-F-CP uptake in tumor predicted the magnitude of the response to subsequent administration of cyclophosphamide. Conclusion: Noninvasive assessment of 18F-F-CP uptake using PET may potentially be helpful for predicting the response of breast tumors to cyclophosphamide before therapy begins.

Answer 4:

Bibliographic Information

Combining Agents that Target the Tumor Microenvironment Improves the Efficacy of Anticancer Therapy. Blansfield, Joseph A.; Caragacianu, Diana; Alexander, H. Richard, III; Tangrea, Michael A.; Morita, Shane Y.; Lorang, Dominique; Schafer, Peter; Muller, George; Stirling, David; Royal, Richard E.; Libutti, Steven K. Tumor Angiogenesis Section, Surgery Branch, National Cancer Institute, NIH, Bethesda, MD, USA. Clinical Cancer Research (2008), 14(1), 270-280. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 148:552920 AN 2008:8763 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: Over the past 60 years, cytotoxic chemotherapy has targeted the cancer cell. Despite this, there have been few cancer cures. A new approach to cancer therapy is to target the multicellular biol. entity of the tumor microenvironment. Exptl. Design: Lenalidomide, an immunomodulatory drug, sunitinib, a tyrosine kinase inhibitor, and low-dose metronomic cyclophosphamide, were tested alone and in combination for their abilities to inhibit endothelial cell tube formation, rat aortic ring outgrowth, tumor growth, and metastatic development in mice. In addn., ectopic tumor lysates were evaluated for the presence of proangiogenic proteins. RESULTS: The three agents alone were shown to significantly inhibit endothelial cells' ability to form tubes and significantly inhibit the multicellular microenvironment in the rat aortic ring assay ($P < 0.01$ and $P < 0.001$). This effect was also significantly augmented when the agents were combined. Furthermore, the three-drug combination was able halt the progression of tumor growth almost completely in xenograft models of ocular melanoma, colon cancer, pancreatic cancer, and cutaneous melanoma. These agents significantly decrease the no. of proliferating cells in tumors, significantly increase the no. of cells undergoing active cell death in tumors, and significantly decrease the no. of blood vessels in treated tumors ($P < 0.05$). Combination therapy shows a decrease in the compensatory up-regulation of proangiogenic proteins after treatment when compared with single-agent therapy. CONCLUSIONS: This combination of agents causes an inhospitable microenvironment for tumor cells and shows great promise for use in the clinic.

Answer 5:

Bibliographic Information

Chemoprotective and adjuvant effects of immunomodulator ginsan in cyclophosphamide-treated normal and tumor bearing mice. Shim, J. Y.; Han, Y.; Ahn, J. Y.; Yun, Y. S.; Song, J. Y. Laboratory of Radiation Immunology, Korea Institute of Radiological and Medical Sciences, Seoul, S. Korea. International Journal of Immunopathology and Pharmacology (2007), 20(3), 487-497. Publisher: Biolife s.a.s., CODEN: IJIPE4 ISSN: 0394-6320. Journal written in English. CAN 148:112483 AN 2007:1232028 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Ginsan is a polysaccharide extd. from Panax ginseng that is known to have multiple immunomodulatory effects. This study evaluates the chemoprotective effect of ginsan on normal mice and the adjuvant effect on tumor bearing mice in combination with cyclophosphamide (CP). Ginsan (100 mg/kg) was injected 24 h before or after a sublethal dose of a CP treatment. The mice pre-treated with ginsan all died within 10 days whereas up to 53% of the mice post-treated with ginsan increased survival to day 30 compared with only 10% in the CP alone treated group on day 30. The post-treatment of ginsan accelerated the recovery of the bone marrow cells and blood neutrophils by approx. 1.3- and 1.75-fold compared to CP treated control mice at 5 days after CP administration, resp. These marked differences in activity between the pre- and post-treatment of ginsan with CP was clarified by examg. the mRNA expression levels of several cytokines in spleen cells and the self-renewal potential of hematopoietic progenitor cells, CFU-s. The post-treatment with ginsan increased the mRNA expression levels of TNF-α, IL-1β, IL-6, SCF, and GM-CSF with respect to that of the CP alone or ginsan pre-treated group. Similarly, the no. of CFU-s was significantly higher in the mice post-treated with ginsan. The inhibition of tumor growth and survival elongation was also obsd. when ginsan was administered 24 h after the CP treatment. These results show that the post-treatment with ginsan had an immunomodulating and adjuvant effect in combination with CP, which indicates its wide applications in reducing the adverse effects of chemotherapy and improving the general conditions of patients.

Answer 6:

Bibliographic Information

Early assessment of therapy response in malignant lymphoma with the thymidine analogue [18F]FLT. Buck, Andreas K.; Kratochwil, Clemens; Glatting, Gerhard; Juweid, Malik; Bommer, Martin; Tepsic, Djurdja; Vogg, Andreas T. J.; Mattfeldt, Torsten; Neumaier, Bernd; Moeller, Peter; Reske, Sven N. Department of Nuclear Medicine, University Hospital Ulm, Ulm, Germany. European Journal of Nuclear Medicine and Molecular Imaging (2007), 34(11), 1775-1782. Publisher: Springer, CODEN: EJNMA6 ISSN: 1619-7070. Journal written in English. CAN 148:208999 AN 2007:1186920 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose: The aim of this study was to det. whether the thymidine analog 3'-deoxy-3'-[18F]fluorothymidine ([18F]FLT) is adequate for early evaluation of the response of malignant lymphoma to antiproliferative treatment in a mouse xenotransplant model. Methods: Immunodeficient mice bearing a follicular lymphoma xenotransplant were treated with high-dose chemotherapy (cyclophosphamide, n = 10), immunotherapy (CD20 mAb, ibritumomab-tiuxetan, n = 10) or radioimmunotherapy ([90Y]CD20 mAb, Zevalin, n = 10). Forty-eight hours after treatment, antiproliferative effects were assessed with [18F]FLT. Ninety minutes after i.v. injection of 5-10 MBq [18F]FLT, mice were sacrificed and radioactivity within the tumor and normal organs was measured using a gamma counter and calcd. as % ID/g. The proliferation fraction in tissue samples derived from treated and untreated tumors was evaluated by Ki-67 immunohistochem., which served as the ref. for proliferative activity. Results: In untreated lymphoma, the mean proliferation fraction was 83.6%. After chemotherapy, the mean proliferation fraction decreased to 39.3% (p = 0.0001), after immunotherapy to 77.6% (p = 0.0078) and after radioimmunotherapy to 78.8% (p = 0.014). In none of the animals was a significant change in tumor size obsd. In untreated lymphoma, tumoral [18F]FLT uptake was 5.4% ID/g, after chemotherapy it was 1.5% (p = 0.0005), after immunotherapy, 3.9% (non-significant), and after radioimmunotherapy, 5.8% (non-significant). Conclusion: In a lymphoma xenotransplant model, [18F]FLT detects early antiproliferative drug activity before changes in tumor size are visible. These findings further support the use of [18F]FLT-PET for imaging early response to treatment in malignant lymphoma.

Answer 7:

Bibliographic Information

The effects of various chemotherapy regimens on the expression of PCNA and Bcl-2 in human breast cancer xenograft (MCF-7) transplanted in nude mice. Wang, Yu-dong; Liu, Wei; Ji, Zhi-min; Zhang, Zhi-gang; Lv, Ya-lei; Wang, Shu-qin. Department of Medical Oncology, The 4th Hospital of Hebei Medical University, Shijiazhuang, Peop. Rep. China. Linchuang Zhongliuxue Zazhi (2007), 12(3), 173-176. Publisher: Institution of Chinese Clinical Oncology Journal, CODEN: LZZIA5 ISSN: 1009-0460. Journal written in Chinese. CAN 148:205626 AN 2007:1152600 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The objective of the paper is to investigate the effects of various chemotherapy regimens on the expression of PCNA and Bcl-2 of breast cancer, to assess the relationships between chemotherapy and two markers, and to evaluate the value of them to predict the response of chemotherapy. Forty-eight nude mice models of human breast cancer xenograft (MCF-7) were established, and then were randomly divided into control and 5 chemotherapy groups (each group, n = 8). Among 5 chemotherapy groups, mice were treated i.p. or orally by 5 chemotherapy regimens (CMF, CAF, NP, TP, Xeloda) resp. at two-thirds LD10 (dose lethal to 10% of the mice). Control animals were administered i.p. with normal saline. The pathol. feature of transplanted tumor was studied by HE stain, and the expression of Bcl-2 and PCNA was studied by SP immunohistochem. method. The expression of PCNA in 5 chemotherapy group was significantly lower than that of control ($P<0.05$), and the expression of PCNA in NP, TP and Xeloda groups was significantly lower than that of CMF and CAF groups ($P<0.05$). Moreover, the expression of PCNA was significantly correlated with pathol. therapeutic response ($P=0.001$). The expression of Bcl-2 in CAF, NP, TP, Xeloda groups was significantly higher than that of control ($P<0.05$). Moreover, the expression of Bcl-2 in TP group was significantly higher than that of CMF and CAF groups ($P<0.05$). The expression of Bcl-2 was not significantly correlated with the pathol. therapeutic response ($P=0.093$). Chemotherapy can increase the expression of PCNA, and decrease the expression of Bcl-2. Different chemotherapy regimens have different effects on PCNA and Bcl-2. PCNA can become a factor to evaluate the response to chemotherapy, and become possibly the prospective factor of chemoselect.

Answer 8:

Bibliographic Information

Inhibitory effects of combined low-dose chemotherapy on angiogenesis and growth of Lewis lung carcinoma xenografts in mice. Qiu, Meng; Yi, Cheng; Hou, Mei. West China Hospital, Sichuan University, Chengdu, Peop. Rep. China. Sichuan Daxue Xuebao, Yixueban (2006), 37(4), 534-537. Publisher: Sichuan Daxue Xuebao, Yixueban Bianjibu, CODEN: SDXYAY ISSN: 1672-173X. Journal written in Chinese. CAN 147:398005 AN 2007:852362 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Antiangiogenic and antitumor effects of combined low-dose cyclophosphamide (CTX) and paclitaxel (PTX) were investigated. In this expt., Lewis lung carcinoma model was established in C57BIL6 mice. Forty mice were randomly divided into four groups: control group, cyclophosphamide (170 mg/kg, q6d) group, paclitaxel (10 mg/kg, q7d) group and cyclophosphamide plus paclitaxel group. The growth of tumor and side effect of each therapy were investigated. Microvessel d. (MVD) was assessed by CD31 immunostaining, and immunohistochem. (IHC) image anal. was performed for semiquantification of vascular endothelial growth factor (VEGF). The combined low-dose therapy with cyclophosphamide and paclitaxel was most effective for antagonizing tumor-assocd. angiogenesis, and the mice of this group had the lowest MVD and VEGF expression, compared with mice of the other groups ($P<0.005$). The combination therapy also brought about higher antitumor rate, lower tumor vol. and lower tumor wt. than did the single therapies ($P<0.005$). The paclitaxel (10 mg/kg, q7d) therapy had the slightest side-effects, and the other therapies had similar acceptable side effects. The combined use of low dose cyclophosphamide and paclitaxel has synergistic antiangiogenic effect on mouse model of Lewis lung carcinoma, and the combination of these two agents is clearly more effective for inhibiting angiogenesis and growth of tumor.

Answer 9:

Bibliographic Information

A New Model of Patient Tumor-Derived Breast Cancer Xenografts for Preclinical Assays. Marangoni, Elisabetta; Vincent-Salomon, Anne; Auger, Nathalie; Degeorges, Armelle; Assayag, Franck; de Cremoux, Patricia; de Plater, Ludmilla; Guyader, Charlotte; De Pinieux, Gonzague; Judde, Jean-Gabriel; Rebucci, Magali; Tran-Perennou, Carine; Sastre-Garau, Xavier; Sigal-Zafrani, Brigitte; Delattre, Olivier; Dieras, Veronique; Poupon, Marie-France. U612, Pharmacologie Preclinique Antitumorale, Institut National de la Sante et de la Recherche Medicale, Fr. Clinical Cancer Research (2007), 13(13), 3989-3998. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 147:397725 AN 2007:718559 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: To establish a panel of human breast cancer (HBC) xenografts in immunodeficient mice suitable for pharmacol. preclin. assays. Exptl. Design: 200 samples of HBCs were grafted into Swiss nude mice. Twenty-five transplantable xenografts were established (12.5%). Their characterization included histol., p53 status, genetic anal. by array comparative genomic hybridization, gene expression by Western blotting, and quant. reverse transcription-PCR. Biol. profiles of nine xenografts were compared with those of the corresponding patient's tumor. Chemosensitivities of 17 xenografts to a combination of Adriamycin and cyclophosphamide (AC), docetaxel, trastuzumab, and Degarelix were evaluated. RESULTS: Almost all patient tumors established as xenografts displayed an aggressive phenotype, i.e., high-grade, triple-neg. status. The histol. of the xenografts recapitulated the features of the original tumors. Mutation of p53 and inactivation of Rb and PTEN proteins were found in 83%, 30%, and 42% of HBC xenografts, resp. Two HBCx had an ERBB2 (HER2) amplification. Large variations were obsd. in the expression of HER family receptors and in genomic profiles. Genomic alterations were close to those of original samples in paired tumors. Three xenografts formed lung metastases. A total of 15 of the 17 HBCx (88%) responded to AC, and 8 (47%) responded to docetaxel. One ERBB2-amplified xenograft responded to trastuzumab, whereas the other did not. The drug response of HBC xenografts was concordant with that of the patient's tumor in five of seven analyzable cases. CONCLUSIONS: This panel of breast cancer xenografts includes 15 triple-neg., one ER pos. and 2 ERBB2 pos. This panel represents a useful preclin. tool for testing new agents and protocols and for further exploration of the biol. basis of drug responses.

Answer 10:

Bibliographic Information

Protection of Lactobacillus on toxicity of cyclophosphamide in chemotherapy. Tang, San-yuan; Li, Jie-ping; Cao, Jian-guo; Wu, You-hua. The First Affilliated Hospital, Nanhua Uriverstity, Hengyang, Hunan, Peop. Rep. China. Hainan Yixue (2007), 18(5), 137-138. Publisher: Hainan Yixue Zazhishe, CODEN: HYAIAX ISSN: 1003-6350. Journal written in Chinese. CAN 147:138213 AN 2007:546287 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This paper studied the protection of Lactobacillus on toxicity of cyclophosphamide in in Balb/c-nu mice bearing human colon cancer xenograft HT-29 cell. The human colon cancer cell xenograft models were established. High-dose cyclophosphamide was injected into the abdominal cavities of model mice, and Lactobacillus was perfused into stomach of model mice. After administration, body wt., white blood cell, serum lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, creatinine, and blood urea nitrogen were resp. detected. Comparison of the differences was made among groups. Higher body wt., higher white blood cell, lower serum lactate dehydrogenase, lower alanine aminotransferase, lower aspartate aminotransferase, lower creatinine, lower blood urea nitrogen were detected in these groups administrated by high-dose cyclophosphamide and Lactobacillus, contrasting to the group administrated by high-dose cyclophosphamide alone, showing a significant difference ($P < 0.05$-0.001) between the groups and pos. correlation to dose of Lactobacillus. In conclusion, Lactobacillus has many protection effects on toxicity of cyclophosphamide, and it can decrease hepatotoxicity, nephrotoxicity and myelosuppression of chemotherapy.

Answer 11:

Bibliographic Information

Anticancer Therapies Combining Antiangiogenic and Tumor Cell Cytotoxic Effects Reduce the Tumor Stem-Like Cell Fraction in Glioma Xenograft Tumors. Folkins, Chris; Man, Shan; Xu, Ping; Shaked, Yuval; Hicklin, Daniel J.; Kerbel, Robert S. Department of Molecular and Cellular Biology Research, Sunnybrook Health Sciences Centre, and Department of Medical Biophysics, University of Toronto, Toronto, ON, Can. Cancer Research (2007), 67(8), 3560-3564. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 146:454195 AN 2007:426093 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Vascular endothelial cells were identified as a crit. component of the neural stem cell niche, raising the possibility that brain tumor stem-like cells (TSLC) may also rely on signaling interactions with nearby tumor vasculature to maintain their stem-like state. The disruption of such a TSLC vascular niche by an antiangiogenic therapy could result in loss of stemness characteristics assocd. with intrinsic drug resistance and, thus, preferentially sensitize TSLC to the effects of chemotherapy. Considering these possibilities, we investigated the impact of antiangiogenic anticancer therapy on the TSLC fraction of glioma tumors. Athymic nude mice bearing s.c. tumor xenografts of the C6 rat glioma cell line were treated with either a targeted antiangiogenic agent, antiangiogenic schedules of low-dose metronomic chemotherapy, combination therapies of antiangiogenic agents and chemotherapy, or, for the purpose of comparison, a conventional cytotoxic schedule of max. tolerated dose chemotherapy using cyclophosphamide. Targeted antiangiogenic therapy or cytotoxic chemotherapy did not reduce the fraction of tumor sphere-forming units (SFU) in the tumor, whereas all treatment groups that combined both antiangiogenic and cytotoxic drug effects caused a significant redn. in SFU. This work highlights the possibility that selective eradication of TSLC may be achieved by targeting the tumor microenvironment (and potentially a supportive TSLC niche) rather than the TSLC directly. Furthermore, this work suggests a possible novel effect of antiangiogenic therapy, namely, as a chemosensitizer of TSLC, and thus represents a possible new mechanism to explain the ability of antiangiogenic therapy to enhance the efficacy of chemotherapy.

Answer 12:

Bibliographic Information

Effects of various chemotherapy regimens on the expression of PCNA and growth of human breast cancer xenograft (MCF-7) in nude mice. Wang, Yu-dong; Liu, Wei; Ji, Zhi-min; Zhang, Zhi-gang; Wang, Jun-ling; Yan, Xia; Zhang, Xiang-hong. Department of Medical Oncology, 4th Hospital, Hebei Medical University, Shijiazhuang Hebei, Peop. Rep. China. Zhongguo Aizheng Zazhi (2007), 17(2), 139-143. Publisher: Fudan Daxue Fushu Zhongliu Yiyuan, CODEN: ZAZHAF ISSN: 1007-3639. Journal written in Chinese. CAN 147:86596 AN 2007:395164 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Although standardized therapy has been widely adapted in clin. practice and results are being improved, effective protocols for truly individualized chemotherapy is still lacking. The anti-tumor activity of different combination regimens on human breast cancer xenograft (MCF-7) transplanted in nude mice and their impacts on the expression of PCNA were investigated, and to evaluate the value of PCNA as predictive factors for the res. 88 Nude mice with human breast cancer xenograft (MCF-7) were randomly divided into control and 10 chemotherapy groups, and 8 mice were assigned into each group. Among 5 chemotherapy groups, they were treated either i.p. or orally by 5 different combinations of chemotherapy regimens (CMF, CAF, NP, TP, Xeloda) at one-third of LD10 dosage, and another 5 chemotherapy groups were treated at two-third . Control animals were given normal saline i.p. The body wt. of nude mice and transplanted tumor growth were recorded on a regular basis, and tumor growth inhibition was calcd. The pathol. features of the transplanted tumor were studied under the microscope before and after treatment. The expression of PCNA was evaluated by SP immunohistochem. method and flow cytometry. The results show that body wt. and tumor wt. of nude mice treated by two-third LD10 dosage of various chemotherapy combinations were significantly lower than that in the control ($P<0.05$), and the inhibition rate of tumor growth for the groups we. The results showed that the two-third LD10 dosage of chemotherapy could reflect the anti-tumor effect of various combinations chemotherapy better and more accurately, so this dosage was used for the next study. The expression at PCNA by immunohistochem. studies shows that the expression of PCNA in every chemotherapy group was significantly lower than that of the control ($P<0.05$).

Moreover, the expressions of PCNA in NP group was significantly lower than that of CMF, CAF, TP and Xeloda group (P<0.05), while TP and Xeloda group was significantly lower than that of CMF and CAF group (P<0.05). FCM anal. shows that FI value of PCNA in every chemotherapy group was significantly lower than that of the control (P<0.05). FI value of PCNA in TP and Xeloda group was significantly lower than that of CMF and CAF group (P<0.05), while NP group a significantly lower than that of CMF group (P<0.05). Relationship between PCNA expression and pathol. response shows that the expression of PCNA was pos. correlated with pathol. therapeutic response of transplanted breast carcinoma (r=0.540, P<0.05). It was concluded that in vivo chemosensitivity testing with two third LD10 dosage of various combinations of chemotherapy cancer could somewhat predict the clin. situations. All of various chemotherapy regimens can decrease the expression of PCNA in breast cancer. The expression of PCNA could perhaps serve as the factor to judge the response to chemotherapy, and play a role in the selection of the kind of chemotherapy to be used in the clinic.

Answer 13:

Bibliographic Information

Inhibitory effects of fumagillol combined with cyclophosphamide on metastasis of lung adenocarcinoma cell line LA795 xenograft in mice. Wang, Xiaohua; Wang, Zheng; Duan, Baochun; Song, Jietao; He, Jianbin; Ou, Liwen; Zhang, Ping. The First Affiliated Hospital, Nanhua University, Hengyang, Hunan Province, Peop. Rep. China. Aizheng (2005), 24(12), 1448-1452. Publisher: Sun Yat-sen Daxue, Aizheng Zhongxin, CODEN: AIZHE4 ISSN: 1000-467X. Journal written in Chinese. CAN 146:220372 AN 2006:1260327 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The synergetic inhibitory effects of fumagillol (TNP-470) in combination with cyclophosphamide (CTX) on metastasis of lung adenocarcinoma cell line LA795 xenograft in mouse were investigated to explore the related mechanism of suppressing tumor metastasis by TNP-470. Forty T739 nude mice bearing highly metastatic LA795 cells were randomized into 5 groups: the control group, vehicle group, TNP-470 (30 mg/kg) group, CTX (40 mg/kg) group and combination group (TNP-470 plus CTX). After killed 3 wk later, the s.c. tumors were weighted to calc. inhibitory rate. The metastatic tumor foci on lung surface in mice were counted to calc. occurrence rate and inhibitory rate of metastases on lung surface. The microvessel d. (MVD) and the expression of tumor metastasis-related factor P-selectin in s.c. tumor were detected by immunohistochem. and analyzed with image anal. system. The inhibitory rate of tumor was significantly higher in combination group (81.5%) than in other groups. TNP-470 plus CTX showed synergetic effects on inhibiting metastasis on lung surface with a Q value of 1.21. The metastatic foci on lung surface were significantly fewer in combination group, TNP-470 group and CTX group than in the control group (1.75±1.71, 4.75±3.34 and 8.50±2.67 vs. 12.13±4.02). The MVD and the expression of P-selectin in s.c. tumor were also significantly lower in combination group and TNP-470 group than in the control group (9.13±1.61 and 12.13±2.84 vs. 20.50±3.12; 5.25±2.27 and 7.13±3.01 vs. 13.75±3.38). It indicated TNP-470 and CTX had synergetic inhibitory effects on lung metastasis of LA795 xenograft tumor. TNP-470 might inhibit lung metastasis of LA795 xenograft tumor by suppressing the expression of P-selectin.

Answer 14:

Bibliographic Information

Application of chimerism-based drug-induced tolerance to rat into mouse xenotransplantation. Tomita, Y.; Shimizu, I.; Iwai, T.; Zhang, Q.-W.; Okano, S.; Kajiwara, T.; Onzuka, T.; Tominaga, R. Cardiovascular Surgery, Kyushu University, Fukuoka, Japan. Scandinavian Journal of Immunology (2006), 64(4), 392-397. Publisher: Blackwell Publishing Ltd., CODEN: SJIMAX ISSN: 0300-9475. Journal written in English. CAN 146:182894 AN 2006:1199405 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The current crit. shortage of human donor organs has stimulated the feasibility of the xenogenic transplantation, such as swine to primate. We have previously reported the induction of donor-specific tolerance in MHC-disparated recipient mice by using our cyclophosphamide (CP)-induced tolerance conditioning. In this study, we examd. the efficacy of our CP-induced tolerance

conditioning in xenogenic transplantation model. F344 rats and B10 mice were used as donors and recipients. Recipient mice were treated with donor spleen cells, CP, Busulfan and bone marrow cells, with or without prior NK-cell depletion. Donor mixed chimerism, and the presence of donor reactive T-cell population were analyzed by flow cytometry. The survival of the donor skin grafts were obsd. after the conditioning. Donor mixed chimerism was temporary induced but terminated at 10 wk after treatments. Donor-specific prolongation of the skin graft survival was obsd. after the treatments, however, grafts were rejected in the long term. NK-cell depletion, prior to the treatments, did not affect the levels of the mixed chimerism or graft prolongation. The donor-reactive recipient T-cell population was remained the same level as the untreated mice, suggesting the failure of the induction of the central T-cell tolerance. Thus, partial efficacy of our CP-induced tolerance treatments in the rat to mice xenotransplantation was obsd. Our results suggested that the addnl. treatments were required to establish the stable xenogenic tolerance.

Answer 15:

Bibliographic Information

Inhibitory effect of tyroserleutide on nude mice transplanted tumor of hepatic carcinoma human BEL-7402. Wang, Li; Lu, Rong; Wang, Li-ming; Zhao, Lin; Fu, Zheng; Wang, Song; Li, Hui-qiang; Yang, Hai-xian; Zhang, Ming-fang; Jin, Meng-jue; Yao, Zhi. Department of Immunology, Tianjin Medical University, Tianjin, Peop. Rep. China. Zhongguo Xinyao Yu Linchuang Zazhi (2005), 24(11), 857-861. Publisher: Zhongguo Xinyao Yu Linchuang Zazhi Zazhishe, CODEN: ZXYLBE ISSN: 1007-7669. Journal written in Chinese. CAN 146:330012 AN 2006:824265 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The aim of the present study was to investigate the antitumor effect of tyroserleutide on the growth of human BEL-7402 hepatic carcinoma inoculated into nude mice and to explore the preliminary mechanism. The nude mice bearing xenograft of the human BEL-7402 hepatic carcinoma were randomly divided into five groups with twelve mice for each, and were given i.p. tyroserleutide,cyclophosphamide,saline or mixt. of amino resp. after tumor implantation. Apoptosis and necrosis were detd. by fluorescence-activated cell sorter(FACS) and cellular microstructural changes were detected by electron microscopy. Tyroserleutide could significantly induce apoptosis, changes of ultrastructure and cell cycle arrest of tumor cell. At doses of 80μg.bul.kg-1 .bul.d-1 and 160μg.bul.kg-1 .bul.d-1, it could significantly inhibit tumor growth in nude mice by inhibition rates of 42% and 58% resp. Tyroserleutide can inhibit significantly the growth of tumor in nude mice. The growth inhibition of the xenografts may concern with the apoptosis of tumor induced by tyroserleutide.

Answer 16:

Bibliographic Information

The combination of the proteasome inhibitor bortezomib and the Bcl-2 antisense molecule oblimersen sensitizes human B-cell lymphomas to cyclophosphamide. O'Connor, Owen A.; Smith, Emily A.; Toner, Lorraine E.; Teruya-Feldstein, Julie; Frankel, Stanley; Rolfe, Mark; Wei, Xiaohui; Liu, Shujun; Marcucci, Guido; Chan, Kenneth K.; Chanan-Khan, Asher. Department of Medicine, Lymphoma, and Developmental Chemotherapy Service, Laboratory of Experimental Therapeutics for Lymphoproliferative Disorders, Memorial Sloan Kettering Cancer Center, New York, USA. Clinical Cancer Research (2006), 12(9), 2902-2911. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 145:388835 AN 2006:532575 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose: To det. whether the combination of the proteasome inhibitor bortezomib and the bcl-2 antisense mol. oblimersen can sensitize human lymphoma to cyclophosphamide. Exptl. Design: Cytotoxicity assays were conducted to det. if there was any additive or synergistic interaction between the combinations of bortezomib, oblimersen, and cyclophosphamide using a std. trypan blue exclusion assay. Based on these expts., in vivo expts. in severe combined immunodeficiency beige mice were done using human lymphoma xenografts in which different schedules were explored. Bcl-2 and oblimersen levels were detd. in treated tumors, some of which were resected at the end of the in vivo expt. and evaluated pathol. Results: The results suggest that the combination of bortezomib and

oblimersen seem to interact in at least an additive fashion, and that the addn. of cyclophosphamide to this drug combination can markedly improve tumor cell kill. In addn., it seems that these drug combinations may be schedule-dependent, with a requirement for oblimersen pretreatment. Animals treated with the triplet drug combination in a schedule-dependent manner experienced pathol. complete regression of disease, which was not obsd. in other treatment cohorts. The addn. of bortezomib also seemed to increase the levels of intracellular oblimersen, which resulted in a marked redn. in Bcl-2. Histol. studies confirmed marked necrosis and caspase-3 activation only in the cohort receiving all three drugs. Conclusion: The use of Bcl-2-directed therapy and a proteasome inhibitor sensitizes human lymphoma cells to cytotoxic drugs like cyclophosphamide. This combination may offer new opportunities for integrating novel targeted therapies with conventional chemotherapy.

Answer 17:

Bibliographic Information

Lactandrate: a D-homo-aza-androsterone alkylator in the treatment of breast cancer. Trafalis, Dimitrios T. P.; Geromichalos, George D.; Koukoulitsa, Catherine; Papageorgiou, Athanasios; Karamanakos, Panayiotis; Camoutsis, Charalambos. Laboratory of Medicinal Chemistry, Faculty of Pharmacy, University of Patras, Patras, Greece. Breast Cancer Research and Treatment (2006), 97(1), 17-31. Publisher: Springer, CODEN: BCTRD6 ISSN: 0167-6806. Journal written in English. CAN 145:410138 AN 2006:467778 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The sensitivity of breast neoplasms to hormonal control provides the basis of novel investigational treatments with steroidal alkylators. An androsterone D-lactam steroidal ester, the 3β-hydroxy-13α-amino-13,17-seco- 5α-androstan-17-oic-13,17-lactam, p-bis(2-chloroethyl)amino Ph acetate (lactandrate) was synthesized and tested for antitumor activity against six human breast cancer cell lines in vitro and against two murine and one xenograft mammary tumors in vivo. A docking study on the binding interactions of lactandrate with the ligand-binding domain (LBD) of estrogen receptor-alpha (ERα) was inquired. In vitro testing of lactandrate cytostatic and cytotoxic activity was performed on T47D, MCF7, MDA-MB-231, BT-549, Hs578T, MDA-MB-435 breast adenocarcinoma human cell lines. In vivo testing was performed on two murine mammary tumors, the MXT tumor and CD8F1 adenocarcinoma, as well as on human mammary carcinoma MX-1 xenograft. Mol. modeling techniques were adopted to predict a possible location and interaction mode of the mol. into LBD. Lactandrate induced significantly high antitumor effect against all tested in vitro and in vivo models. The cell lines with pos. ER expression found to be significantly more sensitive to lactandrate. Moreover, lactandrate found to be positioned inside the binding cavity with its steroidal moiety, while the alkylating moiety protrudes out of receptor's pocket. Lactandrate produced important anticancer activity on breast cancer in vitro and in vivo. Some correlation between ER and lactandrate effect was demonstrated. Docking studies provide the basis for the structure-based design of improved steroidal alkylating esters for the treatment of estrogen-related cancers.

Answer 18:

Bibliographic Information

Colony-Stimulating Factor-1 Antibody Reverses Chemoresistance in Human MCF-7 Breast Cancer Xenografts. Paulus, Patrick; Stanley, E. Richard; Schaefer, Romana; Abraham, Dietmar; Aharinejad, Seyedhossein. Laboratory for Cardiovascular Research, Department of Anatomy and Cell Biology, Vienna Medical University, Vienna, Austria. Cancer Research (2006), 66(8), 4349-4356. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 144:404857 AN 2006:350676 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Overexpression of colony-stimulating factor-1 (CSF-1) and its receptor in breast cancer is correlated with poor prognosis. Based on the hypothesis that blockade of CSF-1 would be beneficial in breast cancer treatment, we developed a murinized, polyethylene glycol-linked antigen-binding fragment (Fab) against mouse (host) CSF-1 (anti-CSF-1 Fab). Mice bearing human, chemoresistant MCF-7 breast cancer xenografts were treated with combination chemotherapy (CMF: cyclophosphamide, methotrexate, 5-fluorouracil;

cycled twice i.p.), anti-CSF-1 Fab (i.p., cycled every 3 days for 14 days), combined CMF and anti-CSF-1 Fab, or with Ringer's soln. as a control. Anti-CSF-1 Fab alone suppressed tissue CSF-1 and retarded tumor growth by 40%. Importantly, in combination with CMF, anti-CSF-1 Fab reversed chemoresistance of MCF-7 xenografts, suppressing tumor development by 56%, down-regulating expression of the chemoresistance genes breast cancer-related protein, multidrug resistance gene 1, and glucosylceramide synthase, and prolonging survival significantly. Combined treatment also reduced angiogenesis and macrophage recruitment and down-regulated tumor matrix metalloproteinase-2 (MMP-2) and MMP-12 expression. These studies support the paradigm of CSF-1 blockade in the treatment of solid tumors and show that anti-CSF-1 antibodies are potential therapeutic agents for the treatment of mammary cancer.

Answer 19:

Bibliographic Information

The effects of thermochemotherapy using cyclophosphamide plus hyperthermia on the malignant pleural mesothelioma in vivo. Riehemann, Kathrin; Schmitt, Oliver; Ehlers, Eva-Maria. Institut fuer Anatomie, Universitaet zu Luebeck, Luebeck, Germany. Annals of Anatomy (2005), 187(3), 215-223. Publisher: Elsevier GmbH, CODEN: ANANEY ISSN: 0940-9602. Journal written in English. CAN 144:80707 AN 2005:1022845 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The human malignant pleural mesothelioma is related to the use of asbestos in the majority of cases. Though the use of asbestos has been prohibited since the 1990s, the incidence of pleural mesothelioma is still increasing because of a latency period of at least 20 years. This study investigated the benefit of single therapy with cyclophosphamide or hyperthermia or the combination of both on cells of a human pleural mesothelioma cell line, xenotransplanted s.c. in the paw of mice. A CONTROL group received the same vol. of physiol. saline. The oxygenation of tumors was measured, tumor growth was followed over 3 wk, immunohistochem. studies and a light and electron microscopic evaluation were performed. Chemotherapy or hyperthermia alone was only temporarily effective. The greatest benefit was achieved using combined thermochemotherapy consisting of cyclophosphamide plus hyperthermia: 50% of this group had partial remissions, and 67% responded to this therapy. After 3 wk tumors grew again. Superior effects could be achieved by performing addnl. cycles of chemotherapy or adding another drug or radiation for instance. This study shows promising results in the treatment of malignant pleural mesothelioma.

Answer 20:

Bibliographic Information

Methionine Aminopeptidase 2 Inhibition Is an Effective Treatment Strategy for Neuroblastoma in Preclinical Models. Morowitz, Michael J.; Barr, Rosalind; Wang, Qun; King, Rebecca; Rhodin, Nicholas; Pawel, Bruce; Zhao, Huaqing; Erickson, Scott A.; Sheppard, George S.; Wang, Jieyi; Maris, John M.; Shusterman, Suzanne. Divisions of Oncology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA. Clinical Cancer Research (2005), 11(7), 2680-2685. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 143:109073 AN 2005:296120 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Tumor vascularity is correlated with an aggressive disease phenotype in neuroblastoma, suggesting that angiogenesis inhibitors may be a useful addn. to current therapeutic strategies. We previously showed that the antiangiogenic compd. TNP-470, an irreversible methionine aminopeptidase 2 (MetAP2) inhibitor, suppressed local and disseminated human neuroblastoma growth rates in murine models but had significant assocd. toxicity at the ED. We have recently shown that a novel, reversible MetAP2 inhibitor, A-357300, significantly inhibits CHP-134-derived neuroblastoma s.c. xenograft growth rate with a treatment-to-control (T/C) ratio at day 24 of 0.19 ($P < 0.001$) without toxicity. We now show that the combination of A-357300 with cyclophosphamide at the maximal tolerated dose sustained tumor regression with a T/C at day 48 of 0.16 ($P < 0.001$) in the CHP-134 xenograft model. A-357300 also significantly inhibited establishment and growth rate of hematogenous metastatic deposits following tail vein inoculation of CHP-134 cells and increased overall survival ($P = 0.021$). Lastly, A-357300 caused regression of established tumors in a genetically engineered murine

model with progression-free survival in five of eight mice ($P < 0.0001$). There was no evidence of toxicity. These data show that MetAP2 may be an important mol. target for high-risk human neuroblastomas. We speculate that the growth inhibition may be through both tumor cell intrinsic and extrinsic (antiangiogenic) mechanisms. The potential for a wide therapeutic index may allow for treatment strategies that integrate MetAP2 inhibition with conventional cytotoxic compds.

Answer 21:

Bibliographic Information

No topoisomerase I alteration in a neuroblastoma model with in vivo acquired resistance to irinotecan. Calvet, L.; Santos, A.; Valent, A.; Terrier-Lacombe, M-J.; Opolon, P.; Merlin, J-L.; Aubert, G.; Morizet, J.; Schellens, J. H. M.; Benard, J.; Vassal, G. Pharmacology and New Treatments in Cancer (UPRES EA 3535), Institut Gustave-Roussy, Villejuif, Fr. British Journal of Cancer (2004), 91(6), 1205-1212. Publisher: Nature Publishing Group, CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 142:169216 AN 2004:824732 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

CPT-11 (irinotecan) is a DNA-topoisomerase I inhibitor with preclin. activity against neuroblastoma (NB) xenografts. The aim was to establish in vivo an NB xenograft resistant to CPT-11 in order to study the resistance mechanisms acquired in a therapeutic setting. IGR-NB8 is an immature NB xenograft with MYCN amplification and 1p deletion, which is sensitive to CPT-11. Athymic mice bearing advanced-stage s.c. tumors were treated with CPT-11 (27 mg kg-1 day-1 × 5) every 21 days (1 cycle) for a max. of four cycles. After tumor regrowth, a new in vivo passage was performed and the CPT-11 treatment was repeated. After the third passage, a resistant xenograft was obtained (IGRNB8-R). The tumor growth delay (TGD) was reduced from 115 at passage 1 to 40 at passage 4 and no complete or partial regression was obsd. After further exposure to the drug, up to 28 passages, the resistant xenograft was definitively established with a TGD from 17 at passage 28. Resistant tumors reverted to sensitive tumors after 15 passages without treatment. IGR-NB8-R remained sensitive to cyclophosphamide and cisplatin and cross-resistance was obsd. with the topoisomerase I inhibitor topotecan. No quant. or qual. topoisomerase I modifications were obsd. The level of expression of multidrug resistance 1 (MDR1), MDR-assocd. protein 1 (MRP1) and, breast cancer resistance protein, three members of the ATP-binding cassette transporter family was not modified over passages. Our results suggest a novel resistance mechanism, probably not involving the mechanisms usually obsd. in vitro.

Answer 22:

Bibliographic Information

Role of various immunocytes in xenograft rejection in mouse-to-rat heart transplantation model. Yang, Guanglun; Huang, Ping; Wei, Zhengqiang; Yao, Zhenxiang. The First Affiliated Hospital, Chongqing Medical University, Chongqing, Peop. Rep. China. Disi Junyi Daxue Xuebao (2003), 24(18), 1685-1687. Publisher: Disi Junyi Daxue Xuebao Bianjibu, CODEN: DJDXEG ISSN: 1000-2790. Journal written in Chinese. CAN 142:315122 AN 2004:684114 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The role of T lymphocytes, natural killer cells (NK) and macrophages (MΦ) in mouse-to-rat xenograft rejection was investigated. Heterotopic cardiac transplantation from mice to rats was performed. The animals were divided into 4 groups: Control, CsA treated, Cyp treated and Cyp+CsA treated. The rejected xenografts were analyzed histol. CD4, CD8, CD57 and CD68 were detected by immunohistochem. The administration of CsA or CyP alone had no appreciable effects on xenograft survival. The combination of CsA and CyP significantly prolonged the xenograft survival than control. The histol. showed a large no. of infiltrating inflammatory cells including CD47+ and CD68+ cells, but not CD4+ or CD8+ cells in the rejected xenografts. NK and MΦ may play an important role in the xenograft rejection in the mouse-to-rat heart transplantation model.

Answer 23:

Bibliographic Information

Effect of ginsenoside Rg3 on the progression of orthotopically xenotransplanted human breast cancer in nude mice and its mechanism. Chen, Dafu; Zhao, Yangbing; Bai, Shaohuai; Shi, Zongdao; Zhang, Jie. Department of General Surgery, The 421th Navy Central Hospital of PLA, Guangzhou, Peop. Rep. China. Sichuan Daxue Xuebao, Yixueban (2003), 34(3), 546-548. Publisher: Sichuan Daxue Xuebao, Yixueban Bianjibu, CODEN: SDXYAY ISSN: 1672-173X. Journal written in Chinese. CAN 141:116665 AN 2004:418529 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The inhibiting effect of ginsenoside Rg3 on the growth and angiogenesis of orthotopically xenotransplanted human breast infiltrating duct carcinoma in nude mice was studied. 15 Female nude mice received xenotransplanted human breast infiltrating duct carcinoma were randomly divided into 3 groups. Ginsenoside Rg3 (5 mg kg-1, qd), cyclophosphamide (CTX; 26 mg kg-1, qod), and control soln. (0.5% Na CM-cellulose, qd) were given to each group by gastrogavage in 0.5 mL vol. for 56 d. Breast cancer masses were collected for light microscope observation. The intra-tumoral microvessel d. (MVD) and the expression of vascular endothelial growth factor (VEGF) were examd. by immunohistochem. staining. The tumor wt. of CTX group was significantly lower than that of control group (P <0.05), and that of Rg3 group was lower than that of control group. The MVD and VEGF of Rg3 group were significantly lower than those of control group (P <0.05). Rg3 could inhibit the growth and angiogenesis of xenotransplanted human breast infiltrating duct carcinoma in nude mice.

Answer 24:

Bibliographic Information

Clonogenic assay with established human tumour xenografts: correlation of in vitro to in vivo activity as a basis for anticancer drug discovery. Fiebig, H. H.; Maier, A.; Burger, A. M. Oncotest GmbH, Institute for Experimental Oncology, Freiburg, Germany. European Journal of Cancer (2004), 40(6), 802-820. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 141:342988 AN 2004:284718 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pluripotent cells can be grown in clonogenic assays. The tumor stem-cell fraction, which accounts for <0.4% of the total cells, and which is considered the most relevant cell type in the development of metastases and recurrences, is able to divide and to form colonies in a semisolid matrix (agar or methylcellulose). Major applications of the tumor clonogenic assay (TCA) are chemosensitivity testing of tumors and xenografts, and for assessments within drug discovery programs. Of crit. relevance for the usefulness of the TCA is whether it can predict sensitivity or resistance towards clin. used agents. When we compared the response of human tumors established as xenografts in nude mice in the TCA in vitro to that of the clin. response, 62% of the comparisons for drug sensitivity, and 92% of the comparisons for drug resistance were correct. The same percentage of true/false observations was found when tumors were tested after serial passage in nude mice in the TCA in vitro and their response compared to in vivo activity in corresponding xenografts (60% and 90%, resp.). The highest correct predictive values were, however, found when the clin. response of tumors was compared to their explants established in the nude mouse and treated in vivo. Of 80 comparisons performed, we obsd. a correct prediction for tumor resistance in 97% and for tumor sensitivity in 90%. In our opinion, the TCA with established human tumor xenografts has an important role in current drug discovery strategies. We therefore included the TCA as secondary assay in our approach to anticancer drug discovery and found that a no. of novel agents were active; these are now in advanced preclin. development or clin. trials. Thus, the tumor clonogenic assay has proven predictive value in the chemosensitivity testing of std. and exptl. anticancer drugs.

Answer 25:

Bibliographic Information

Effect of Ginsenoside Rg3 combined with cytotoxic agent on the progression of xenotransplanted human breast infiltrating duct carcinoma in nude mice. Chen, Da-fu; Zhao, Yang-bing; Bai, Shao-huai; Shi, Zongdao; Jiang, Lili. Dep. General Surgery, West China Hospital, Sichuan University, Chengdu, Peop. Rep. China. Zhongguo Puwai Jichu Yu Linchuang Zazhi (2002), 9(5), 300-302. Publisher: Zhongguo Puwai Jichu Yu Linchuang Zazhi Bianji Weiyuanhui, CODEN: ZJLZFX ISSN: 1007-9424. Journal written in Chinese. CAN 140:280871 AN 2003:761729 CAPLUS

Abstract

The objective was to study the mechanism of reducing the intratumoral microvessel d. (MVD) by ginsenoside Rg3 (Rg3) combined with a cytotoxic agent in xenotransplanted human breast infiltrating duct carcinoma in nude mice. Sixteen female nude mice were randomly divided into 4 groups to receive cyclophosphamide (16 mg/kg, qd) combined with Rg3 (10 mg/kg, qd), Rg3 (10 mg/kg, qd) alone, cyclophosphamide (16 mg/kg, qd) alone, or 0.5% sodium CM-cellulose (0.5 mL, qd) resp., for 55 days. Breast cancer mass was weighed and sampled for light microscopic observation. The intra-tumor MVD was examd. by immunohistochem. staining. The tumor wt. of the treated group was significantly lower than that of control group. The tumor wt. of the Rg3 combined with CTX group was lower than that of Rg3 group. The MVD value of Rg3 group was significantly lower than that of CTX group and control group. The MVD was significantly reduced in the Rg3 combined with CTX group than that in the others. Thus, Rg3 combined with CTX can inhibit the growth of xenotransplanted human breast infiltrating duct carcinoma, and reduce the intratumoral MVD.

Answer 26:

Bibliographic Information

Biodistribution of 131I-, 186Re-, 177Lu-, and 88Y-Labeled hLL2 (Epratuzumab) in Nude Mice with CD22-Positive Lymphoma. Postema, Ernst J.; Frielink, Cathelijne; Oyen, Wim J. G.; Raemaekers, John M. M.; Goldenberg, David M.; Corstens, Frans H. M.; Boerman, Otto C. Department of Nuclear Medicine, UMC Nijmegen, Nijmegen, Neth. Cancer Biotherapy & Radiopharmaceuticals (2003), 18(4), 525-533. Publisher: Mary Ann Liebert, Inc., CODEN: CBRAFJ ISSN: 1084-9785. Journal written in English. CAN 140:317189 AN 2003:692525 CAPLUS

Abstract

Radioimmunotherapy (RIT) is a new and effective treatment modality in patients with non-Hodgkin's lymphoma. The monoclonal antibody (mAb) hLL2 (epratuzumab), a humanized mAb directed against the CD22 antigen, and which internalizes, can be labeled with various radionuclides. The biodistribution of hLL2 labeled with 131I, 186Re, 177Lu, and 88Y was studied in nude mice with s.c. human lymphoma xenografts in order to det. the most suitable of these four radionuclides for RIT with hLL2. Methods: Human Ramos lymphoma xenografts were transplanted in cyclophosphamide-pretreated athymic BALB/c mice. Four groups of mice were injected i.v. with 131I-, 186Re-, 88Y-, or 177Lu-labeled hLL2, resp. To det. the nonspecific tumor uptake, two groups of mice received 88Y-labeled or 131I-labeled control antibody, cG250. The biodistribution of the radiolabel was detd. 1, 3, and 7 days postinjection (p.i.). Results: Radiolabeled hLL2 had a higher tumor uptake than the nonspecific mAb at all time-points, irresp. of the radiolabel used. Tumor accretion of 88Y- and 177Lu-hLL2 was higher than tumor uptake of 131I- and 186Re-hLL2. Activity in the bone, represented by the femur without bone marrow, was higher for 177Lu- and 88Y-hLL2 than for 131I- and 186Re-hLL2 on day 7 p.i. Conclusion: The use of the residualizing radiolabels 88Y and 177Lu in combination with a mAb directed against an internalizing antigen resulted in higher uptake and better retention of the radiolabel in the tumor.

Answer 27:

Bibliographic Information

Antileukemic activity of treosulfan in xenografted human acute lymphoblastic leukemias (ALL). Fichtner, I.; Becker, M.; Baumgart, J. Experimental Pharmacology, Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany. European Journal of Cancer (2003), 39(6), 801-807. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 139:345400 AN 2003:206379 CAPLUS

Abstract

Treosulfan (L-threitol-1,4-bis-methanesulfonate; Ovastat) is a bifunctional alkylating drug indicated for the treatment of advanced ovarian carcinoma. Recent data revealed immunosuppressive characteristics and substantial hematopoietic stem cell toxicity after repeated dosing of mice. Therefore, treosulfan is considered to be an alternative conditioning agent to busulfan (for example) administered prior to allogeneic/autologous stem cell transplantation of patients with hematol. malignancies. An antineoplastic activity for treosulfan has been previously shown in preclin. models of melanoma, breast, lung and renal-cell carcinomas. Here, in vivo antileukemic activity of treosulfan is compared with the activity of equitoxic doses of cyclophosphamide or busulfan for the first time using human acute lymphoblastic leukemia (ALL)-models of pediatric origin xenotransplanted into non-obese diabetic (NOD)/severe combined immunodeficient (SCID) mice. Treosulfan treatment achieved an optimum treated to control (T/C) value of 159% (survival time) against B-ALL-SCID 7 and a T/C value of 0% (tumor growth) against T-ALL-SCID 4 and proB-ALL-SCID 19, resp. Complete regression of established s.c. growing nodules of ALL-SCID 4 and 19 was obvious and long-term survivors without tumor re-growth were obsd. Equitoxic doses of busulfan (ALL-SCID 4, 7, 19) or cyclophosphamide (ALL-SCID 19) were less effective with regard to the nos. of complete regressions and the no. of cured animals. Side-effects included myelotoxicity and a small redn. in body wt., but these were tolerable. Treosulfan can be considered a highly active antileukemic drug whose corresponding clin. value is to be tested in appropriate protocols with leukemic patients.

Answer 28:

Bibliographic Information

O6-benzylguanine-mediated enhancement of chemotherapy. Friedman, Henry S.; Keir, Stephen; Pegg, Anthony E.; Houghton, Peter J.; Colvin, O. Michael; Moschel, Robert C.; Bigner, Darell D.; Dolan, M. Eileen. Department of Surgery, Duke University Medical Center, Durham, NC, USA. Molecular Cancer Therapeutics (2002), 1(11), 943-948. Publisher: American Association for Cancer Research, CODEN: MCTOCF ISSN: 1535-7163. Journal written in English. CAN 139:30329 AN 2003:69745 CAPLUS

Abstract

We have previously demonstrated (A. E. Pegg, Cancer Res., 50: 6119-6129, 1990) that O6-benzylguanine (O6-BG) enhances nitrosourea, temozolomide, and cyclophosphamide activity in malignant glioma xenografts growing in athymic nude mice. More recently, we have demonstrated (V. J. Patel et al., Clin. Cancer Res., 6: 4154-4157, 2000; P. Pourquier et al., Cancer Res., 61: 53-58, 2001) that the combination of temozolomide plus irinotecan (CPT-11) displays a schedule-dependent enhancement of antitumor activity secondary to trapping of topoisomerase I by O6-methylguanine residues in DNA. These studies suggested that there might be favorable therapeutic interactions between O6-BG and combinations of 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) plus cyclophosphamide or temozolomide plus CPT-11, resp. Our present results indicate that the combination of cyclophosphamide plus BCNU plus O6-BG produces growth delays modestly-to-markedly-superior to combinations of cyclophosphamide with BCNU. Although the combination of temozolomide and CPT-11 reveals a marked increase in activity compared with either agent used alone, the addn. of O6-BG to this combination dramatically increased the growth delay of the O6-alkylguanine-DNA alkyltransferase (AGT)-pos. malignant glioma D-456 MG. These results suggest that a Phase I trial of CPT-11 plus temozolomide plus O6-BG in AGT-pos. tumors may be an important intervention to maximize the therapeutic benefits of the combination of CPT-11 and temozolomide.

Answer 29:

Bibliographic Information

Rituximab, cyclophosphamide, dexamethasone (RCD) regimen induces cure in a WSU-WM xenograft model and a partial remission in a previously treated Waldenstrom's macroglobulinemia patient. Mohammad, Ramzi M.; Aboukameel, Amro; Nabha, Sanaa; Ibrahim, Dina; Al-Katib, Ayad. Division of Hematology and Oncology, Department of Internal Medicine, Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, USA. Journal of Drug Targeting (2002), 10(5), 405-410. Publisher: Taylor & Francis Ltd., CODEN: JDTAEH ISSN: 1061-186X. Journal written in English. CAN 138:198246 AN 2002:629464 CAPLUS

Abstract

Waldenstrom's macroglobulinemia (WM) is an uncommon lymphoproliferative disease which remains incurable with current treatment protocols. A permanent WM cell line, WSU-WM, was previously established, which grows as a xenograft in severe combined immunodeficient (SCID) mice. This study investigated the antitumor effects of the rituximab (RTX), cyclophosphamide (CTX), dexamethasone (DEX) [RCD] regimen in vivo in mice with a WSU-WM SCID xenograft and in a patient with WM. For the preclin. efficacy study, WSU-WM-bearing SCID mice received RTX (150 mg/kg/injection i.v.), CTX (90 mg/kg/injection, s.c.) as single agents, or diluent. The combination group received RTX at 150 mg/kg/injection, CTX at 150 mg/kg/injection, and DEX at 1.0 mg/kg/injection, i.v. Tumor growth inhibition, tumor growth delay, and log10 kill (net) were 24.5%, 37 days, and 5.52 for RTX and 88%, 0.0 days, and 0.0 log10 kill for CTX. No cures were obsd. with either agent; however, all the mice (6/6) with bilateral tumors were cured when treated with the RCD regimen. A 57-yr-old patient with relapsed WM was treated with the RCD regimen and showed an excellent partial remission for 7 mo. The patient tolerated the treatment very well, the Hb improved dramatically, platelets remained stable, the IgM level normalized and there was only minimal involvement of bone marrow. Based on these results, the RCD regimen is effective against WM and should be further evaluated in clin. trials.

Answer 30:

Bibliographic Information

Genome-wide cDNA microarray screening to correlate gene expression profiles with sensitivity of 85 human cancer xenografts to anticancer drugs. Zembutsu, Hitoshi; Ohnishi, Yasuyuki; Tsunoda, Tatsuhiko; Furukawa, Yoichi; Katagiri, Toyomasa; Ueyama, Yoshito; Tamaoki, Norikazu; Nomura, Tatsuji; Kitahara, Osamu; Yanagawa, Rempei; Hirata, Koichi; Nakamura, Yusuke. Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, Tokyo, Japan. Cancer Research (2002), 62(2), 518-527. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 136:395496 AN 2002:108259 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

One of the most crit. issues to be solved in regard to cancer chemotherapy is the need to establish a method for predicting efficacy or toxicity of anticancer drugs for individual patients. To identify genes that might be assocd. with chemosensitivity, we used a cDNA microarray representing 23,040 genes to analyze expression profiles in a panel of 85 cancer xenografts derived from nine human organs. The xenografts, implanted into nude mice, were examd. for sensitivity to nine anticancer drugs (5-fluorouracil, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-1-(2-chloroethyl)-1-nitrosourea hydrochloride, adriamycin, cyclophosphamide, cisplatin, mitomycin C, methotrexate, vincristine, and vinblastine). Comparison of the gene expression profiles of the tumors with sensitivities to each drug identified 1,578 genes whose expression levels correlated significantly with chemosensitivity; 333 of those genes showed significant correlation with two or more drugs, and 32 correlated with six or seven drugs. These data should contribute useful information for identifying predictive markers for drug sensitivity that may eventually provide "personalized chemotherapy" for individual patients, as well as for development of novel drugs to overcome acquired resistance of tumor cells to chem. agents.

Answer 31:

Bibliographic Information

Combining radioimmunotherapy and chemotherapy for treatment of medullary thyroid carcinoma: Effectiveness of dacarbazine. Stein, Rhona; Chen, Susan; Reed, Linda; Richel, Heidi; Goldenberg, David M. Garden State Cancer Center, Belleville, NJ, USA. Cancer (New York, NY, United States) (2002), 94(1), 51-61. Publisher: John Wiley & Sons, Inc., CODEN: CANCAR ISSN: 0008-543X. Journal written in English. CAN 136:259269 AN 2002:57632 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Background. To enhance the efficacy of chemotherapy for medullary thyroid carcinoma (MTC), we evaluated the effect of combining radioimmunotherapy (RAIT) with 90Y-anticarcinoembryonic antigen (CEA) monoclonal antibody MN-14 and chemotherapy in nude mice bearing human MTC xenografts. A preliminary study evaluated doxorubicin, dacarbazine (DTIC), cyclophosphamide, and vincristine, singly and in combination, for their effect on the growth of MTC xenografts (TT) in nude mice. Given individually, DTIC yielded the most effective tumor growth inhibition, delaying the mean time to doubling from 1 wk for untreated tumor-bearing mice to 7.5 wk. Administering either the 4 drugs in combination or a 2-drug combination comprised of doxorubicin and DTIC significantly improved the efficacy compared with any single drug alone, increasing the mean doubling time to 10-12 wk. Methods. Drug doses were selected to conform to the doses of each drug given clin. For the combined modality therapy, administration of 90Y-labeled anti-CEA monoclonal antibody MN-14 to nude mice bearing established TT tumors was followed by various chemotherapy regimens initiated 24 h after RAIT. Chemotherapy protocols combined with RAIT included doxorubicin or DTIC alone and in combination, and the doxorubicin, DTIC, cyclophosphamide, and vincristine 4-drug protocol. Tumor vols. were measured weekly, and toxicity was evaluated by measuring blood counts and body wt. Results. Combinations of RAIT and chemotherapy with DTIC or RAIT and chemotherapy with the drug combinations were found to augment the antitumor effects of RAIT or chemotherapy alone, without a significant increase in toxicity. The mean tumor vol. doubling times were increased up to 100% compared with the results of chemotherapy alone. No significant differences in tumor growth were obsd. between the RAIT plus DTIC protocol and the RAIT plus two- or four-drug protocols. Conclusions.

The superiority of the combined modality treatment argues for the integration of RAIT into chemotherapeutic regimens for MTC treatment. Clin. trials are needed to assess these principles in MTC patients.

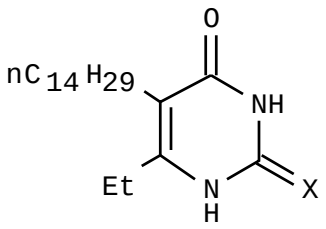
Answer 32:

Bibliographic Information

Design, Synthesis, and Characterization of the Antitumor Activity of Novel Ceramide Analogues. Macchia, Marco; Barontini, Silvia; Bertini, Simone; Di Bussolo, Valeria; Fogli, Stefano; Giovannetti, Elisa; Grossi, Enzo; Minutolo, Filippo; Danesi, Romano. Department of Pharmaceutical Sciences, University of Pisa, Pisa, Italy. Journal of Medicinal Chemistry (2001), 44(23), 3994-4000. Publisher: American Chemical Society, CODEN: JMCMAR ISSN: 0022-2623. Journal written in English. CAN 136:53590 AN 2001:719208 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A deficiency in apoptosis is one of the key events in the proliferation and resistance of malignant cells to antitumor agents; for these reasons, the search for apoptosis-inducing drugs represents a valuable approach for the development of novel anticancer therapies. In this study we report the first example of conformationally restrained analogs of ceramide, where the polar portion of the mol. has been replaced by a thiouracil {[I; X = S (II)], [III; X = S (IV)]} or uracil I [X = O (V)], III [X = O (VI)] ring. The evaluation of their biol. activity on CCRF-CEM human leukemia cells demonstrated that the most active was II followed by V (mean 50% inhibition of cell proliferation [IC50] 1.7 and 7.9 μM, resp.), while compds. IV and VI were inactive, as were uracil, thiouracil, and 5,6-dimethyluracil, the pyrimidine moieties of compds. II, IV-VI. For comparison, the IC50 of the ref. substance, the cell-permeable C2-ceramide, was 31.6 μM. Compds. II and V and C2-ceramide were able to trigger apoptosis, as shown by the occurrence of DNA and nuclear fragmentation, and to release cytochrome c from treated cells. The treatment of female CD-1 nu/nu athymic mice bearing a WiDr human colon xenograft with the most active compd. II at 2, 10, 50, and 200 mg/kg i.p. daily for 10 days resulted in an antitumor effect that was equiv. at 50 mg/kg or superior (200 mg/kg) to that of cyclophosphamide, 20 mg/kg i.p. daily, delivered on the same schedule, with markedly lower systemic toxicity. In conclusion, the present study demonstrates that the new ceramide analogs II and V are characterized by in vitro and in vivo antitumor activity and low toxicity.



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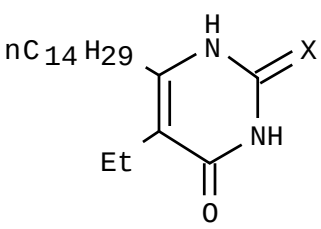


III

Answer 33:

Bibliographic Information

Experimental chemotherapy against canine mammary cancer xenograft in SCID mice and prediction of its clinical effect. Yamashita, Atsuko; Maruo, Kohji; Suzuki, Kaoru; Shirota, Kinji; Kobayashi, Kimio; Hioki, Kyoji. Department of Veterinary Surgery, Tokyo University of Agriculture and Technology, Tokyo, Japan. Journal of Veterinary Medical Science (2001), 63(8), 831-836. Publisher: Japanese Society of Veterinary Science, CODEN: JVMSEQ ISSN: 0916-7250. Journal written in English. CAN 136:379575 AN 2001:706827 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effectiveness of 6 antitumor agents was evaluated for a canine mammary gland tumor (CMG-6) serially transplanted into mice with severe combined immunodeficiency. CMG-6, a solid carcinoma, was s.c. transplanted into immunodeficient mice, and 6 antitumor agents were given i.v. as a single injection. The min. EDs (MEDs; mg/kg) in mice were: cyclophosphamide (CPM) 65, doxorubicin (DXR) 6, cisplatin (CDDP) 5, vincristine (VCR) 1.6, vinblastine (VLB) >5.5, 5-fluorouracil (5-FU) 105. The clin. effects of the drugs were predicted based on the ratio of the area under the curve (AUC) in dogs given a clin. dose (AUC dog) to the AUC of mice given a MED (AUC mouse) from published refs. The AUC ratios were: CPM 2.24, DXR 0.19, CDDP 1.20, VCR 0.04, VLB <1.24 and 5-FU 1.15. The drugs having a value of >1.0 for the AUC dog/AUC mouse ratio were CPM, CDDP and 5-FU, suggesting that they might be effective in the original dogs with CMG-6. Combination chemotherapy using clin. equiv. doses of CDDP and CPM, which had the two highest values of the AUC dog/AUC mouse ratio in single-agent therapy, had addnl. effects as compared to the effectiveness of the single agents against CMG-6.

Answer 34:

Bibliographic Information

Prolongation of xenograft survival using monoclonal antibody CD45RB and cyclophosphamide in rat-to-mouse kidney and heart transplant models. Zhang, Zheng; Lazarovits, Andrew; Gao, Zhuhua; Garcia, Bertha; Jiang, Jifu; Wang, Jiaojing; Xing, Jing-Jing; White, Martin; Zhong, Robert. Departments of Surgery, The University of Western Ontario, ON, Can. Transplantation (2000), 69(6), 1137-1146. Publisher: Lippincott Williams & Wilkins, CODEN: TRPLAU ISSN: 0041-1337. Journal written in English. CAN 133:280319 AN 2000:280881 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Intrigued by the finding that a monoclonal antibody (mAb) directed against the B exon of restricted CD45 (CD45RB mAb) induced renal allograft tolerance in the mouse model, we hypothesized that CD45RB mAb may prevent xenograft rejection. We explored the role of CD45RB mAb in preventing xenograft rejection in rat-to-mouse kidney and heart transplant models. Mice with rat kidney and heart xenografts were treated with a short course of mAb, cyclosporine, cyclophosphamide, or mAb + cyclophosphamide combination therapy. Untreated heart and kidney xenografts served as controls. Untreated controls developed acute vascular and cellular rejection rapidly with a median survival time of only 6 days. Long-term kidney (median survival time = 70 days) and heart xenograft survival (median survival time = 65 days) was achieved using the combination therapy of mAb + cyclophosphamide. One-third of the kidney recipients with combination therapy survived 100 days. Immunohistochem. and xenospecific-antibody anal. demonstrated that combination therapy remarkably reduced IgG and IgM deposition and also inhibited CD4+, CD8+, and Mac-1+ cell infiltration at early stages. This therapy, however, did not induce tolerance in this model as evoked xenoreactive antibodies and cellular responses may be the cause of late xenograft failure. A short course of CD45RB mAb combined with cyclophosphamide effectively inhibits cellular and humoral immunoresponses and remarkably prolongs xenograft survival in rat-to-mouse heart and kidney transplant models.

Answer 35:

Bibliographic Information

Development of human lymphoma/leukemia xenograft models in immune-deficient mice for evaluation of potential

anticancer agents. Dykes, D. J.; Hollingshead, M. G.; Camalier, R. F.; Waud, W. R.; Mayo, J. G. Southern Research Institute, Birmingham, AL, USA. Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 295-304. Publisher: S. Karger AG, CODEN: COONEV ISSN: 0250-3220. Journal written in English. CAN 133:217399 AN 2000:242563 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eleven human lymphoma/leukemia cell lines were assessed as in vivo xenograft models in severe combined immunodeficient (SCID) mice. In prepn. for efficacy evaluations of new antitumor agents, all eleven cell lines have been characterized for sensitivity to known clin. useful agents. The lines included in the study represent a variety of diseases including T-cell, myelogenous, and lymphoblastic leukemias, as well as histiocytic, B-cell and Burkitt's lymphomas. The selected agents for this study were representative of various chem. classes. Addnl., growth studies were performed including comparisons in athymic nude mice. These studies were designed to det. s.c. tumor vol. doubling times, graft success, latent growth periods, and other characteristics necessary to effectively implement and interpret anticancer efficacy evaluations. The various tumor lines used proved to be good models for chemotherapy trials. In the chemotherapy trials, considerable independent chemotherapeutic profiles were obsd. but there were also some similarities among the various histol. types.

Answer 36:

Bibliographic Information

Experimental intestinal transplantation using mouse fetal intestine in the rat: combination effect of FK 506 with cyclophosphamide. Uchida, H.; Kobayashi, E.; Ogino, Y.; Mizuta, K.; Hashizume, K.; Fujimura, A. Division of Organ Replacement Research, Center for Molecular Medicine, Tochigi, Japan. Transplantation Proceedings (1999), 31(7), 2799-2800. Publisher: Elsevier Science Inc., CODEN: TRPPA8 ISSN: 0041-1345. Journal written in English. CAN 132:246017 AN 1999:733752 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study tested the efficacy of a combined regimen of FK 506 and cyclophosphamide using a model of mouse fetal intestinal xenografting without vascular anastomosis. While xenografts failed with support of FK 506 or cyclophosphamide alone, they were accepted by 7 of 10 rats treated with the combined regimen.

Answer 37:

Bibliographic Information

Effects of the antiestrogen EM-800 (SCH 57050) and cyclophosphamide alone and in combination on growth of human ZR-75-1 breast cancer xenografts in nude mice. Gutman, Matthieu; Couillard, Steeve; Labrie, Fernand; Candas, Bernard; Labrie, Claude. Oncology and Molecular Endocrinology Research Center, Centre Hospitalier Universitaire de Quebec and Laval University, Quebec, QC, Can. Cancer Research (1999), 59(20), 5176-5180. Publisher: AACR Subscription Office, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 131:331846 AN 1999:693619 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Human breast cancer proliferates as heterogeneous cell populations that exhibit different sensitivities to therapeutic agents. A logical approach to control these different cancer cell populations is the use of combined treatment with agents that block cell proliferation or induce apoptosis via different mechanisms. We therefore investigated the effect of treatment with the novel pure antiestrogen EM-800, alone or in combination with chemotherapy, on the growth of ZR-75-1 human breast tumors in nude mice, a well-recognized model of human breast cancer. Mice bearing estrone-releasing silastic implants as estrogenic stimulus received EM-800 or cyclophosphamide alone or in combination for 227 days. Cyclophosphamide (256 mg/kg/2 wk) was administered by i.p. injection in 64

mg/kg fractions over 4 consecutive days with repetition of the cycle every 14 days. EM-800 was administered p.o. once daily at the maximally ED of 300 μg/mouse. After 227 days of treatment, av. tumor size in mice receiving estrone alone was 192% higher than pretreatment. The av. tumor size of mice treated with chemotherapy was reduced by 47%, whereas on the other hand, EM-800 caused a 81% decrease of the value of the same parameters. The combined treatment (EM-800 + cyclophosphamide), on the other hand, resulted in a 95% decrease in tumor size compared with control estrogen alone. In fact, EM-800 alone decreased tumor size to 55% of the value at the start of treatment, whereas the addn. of cyclophosphamide to the antiestrogen further decreased tumor size to as low as 15% of the pretreatment value. The combination of EM-800 and cyclophosphamide resulted in 95% of complete or partial responses compared with 61 and 27% with EM-800 and cyclophosphamide alone, resp. In fact, in the combination therapy group, only one tumor remained stable, while 17 regressed >50% and four disappeared. It is noteworthy that no tumor progressed with EM-800 alone or in combination with cyclophosphamide.
The present data show, for the first time, that the addn. of cyclophosphamide to a pure antiestrogen used at a maximal dose causes a more potent inhibition of human breast tumor growth, thus suggesting that combined treatment using a maximal dose of a pure antiestrogen and a chemotherapeutic agent(s), two classes of compds. having different mechanisms of action, could further improve breast cancer therapy above the results achieved with a potent and pure antiestrogen alone in estrogen-sensitive breast cancer.

Answer 38:

Bibliographic Information

Expression of CD44 isoforms in human breast carcinoma xenografts is not influenced by the treatment of mice with cytostatics or (anti-)hormones. Dehmel, A.; Becker, M.; Lemm, M.; Fichtner, I. Max-Delbruck-Center of Molecular Medicine, Berlin, Germany. Anticancer Research (1999), 19(3A), 1977-1987. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 132:120767 AN 1999:654678 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

CD44 std. (s) and variant (v) isoforms have been discussed to be implicated in progression and metastasis of different malignomas. For breast carcinomas, the results of different studies are contradictory. These apparent discrepancies suggest that CD44 isoforms are not available on the tumor cell surface, but could be regulated by different endogenous and exogenous factors. Here we report the regulation of CD44 isoforms in xenografted breast cancer cell lines by cytostatics, hormones and antihormones. The human breast cancer models MDA-MB 435, MCF-7, NCI/ADR, 4296, 4151 and 4134 were transplanted into the mammary fat pad of nude mice. When tumors reached a palpable size, animals were treated with farmorubicin, cyclophosphamide, estradiol, tamoxifen or progesterone, resp. At different times after treatment, serum and tumors were taken. The expression of CD44 and its isoforms was detd. by immunohistochem. and RT-PCR, serum levels were measured by human specific ELISA kits. Serum levels of CD44s and v6 varied among the tumors. For 3/6 tumors we found differences between control groups and treated animals. Immunohistochem. results remained unchanged: each tumor showed a specific pattern of CD44 expression, but this pattern did not change when the animals received cytostatics, hormones or antihormones. The same held true for RT-PCR-results. Also, the time of tumor collection had no influence on CD44 expression. Therefore, it can be concluded, that in the xenografted breast cancer cell lines a regulation of CD44 isoforms by farmorubicin, cyclophosphamide, estradiol, progesterone or tamoxifen could not be found, while serum levels were influenced in some cases probably due to tumor cell kill and shedding of surface proteins into blood stream.

Answer 39:

Bibliographic Information

Antitumor efficacy of combination chemotherapy with UFT and cyclophosphamide against human breast cancer xenografts in nude mice. Haga, Shunsuke; Shimizu, Tadao; Imamura, Hiroshi; Watanabe, Osamu; Kinoshita, Jun; Fukushima, Masakazu; Kajiwara, Tetsuro. Department of Surgery, Tokyo Women's Medical College Daini Hospital, Tokyo, Japan. Anticancer Research (1999), 19(3A), 1791-1796. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 132:117098 AN 1999:654662 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The combination of cyclophosphamide (CPA) and 5-fluorouracil (5-FU) is currently regarded as the most effective therapy for the treatment of patients with advanced and recurrent breast cancer. This study evaluated the augmentation of antitumor activity and toxicity by coadministration of CPA and UFT (1M tegafur - 4M uracil) instead of i.v. 5-FU on H-31 human breast cancer xenografts in nude mice. The max. tolerable dose (MTD) of UFT alone (24 mg/kg) and CPA alone (85 mg/kg) had a significant effect on H-31 tumors in mice, with 86.6% and 83.0% inhibition of tumor growth, resp., and without loss of body wt., diarrhea or myelosuppression. The combined administration of the full and 83.3% MTD of UFT and CPA augmented the antitumor activity compared to that of UFT alone and CPA alone. The ratios of tumor vol. in the UFT-plus-CPA-treated group to the UFT- and CPA-alone treated groups was 0.28 and 0.36, resp., for the full MTD, and 0.51 and 0.67, resp. for the 83.3% MTD. When CPA was consecutively administered to the tumor-bearing mice for 14 days, there were no decreases in the activities of enzymes related to 5-FU metab., but there was a increase in the activity of ribonucleotide reductase, suggesting that anabolism of 5-FU derived from tegafur is accelerated to some extent by coadministration of CPA. These results suggest that combination therapy with oral UFT and CPA may be useful for the long-term treatment of cancer patients with advanced and recurrent breast cancers.

Answer 40:

Bibliographic Information

Antitumor activity of titanocene dichloride in xenografted human renal-cell carcinoma. Kopf-Maier, P. Institut fur Anatomie, Freie Universitat Berlin, Berlin, Germany. Anticancer Research (1999), 19(1A), 493-504. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 131:111022 AN 1999:298101 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Titanocene dichloride [(C5H5)2TiCl2] is a new-developed organometallic antitumor agent which is currently being investigated in clin. trials of phases I and II. In the present study, it was tested for antitumor activity in human renal tumors either growing as monolayers in vitro or as xenografts in athymic mice. For comparison, approved cytostatic drugs (in vitro, vinblastine and 5-fluoro-2'-deoxyuridine; in vivo, cyclophosphamide, vinblastine, and 5-fluorouracil) were administered in vitro and in vivo at equiv. or equitoxic dose levels, resp. Under in vitro conditions, titanocene dichloride was active only moderately. When it was applied at peak plasma level of 104 mol/l, it induced cell growth inhibitions by 25-50% in all KTCTL cell lines investigated (KTCTL-1M, KTCTL-2, KTCTL-26A, KTCTL-30, KTCTL-84). In the N-U 2 carcinoma cell strain it was more effective and caused cell growth inhibitions of 70-80% at the 10-4 mol/l level, the IC50 value amounting to 5 $\times$ 10-6 mol/l. When titanocene dichloride was applied i.p. according to the Q3Dx5 and Q2Dx5 regimens and investigated in the human renal-cell carcinoma N-U 2 growing as xenograft in athymic mice, it brought about significant and dose-dependent growth redns. by 50-75% in relation to untreated controls, whereas cyclophosphamide given as single bolus injection and vinblastine administered both as single and triple doses were slightly less effective in this xenograft. MKT 4 and MKT 5, two formulations of titanocene dichloride which are currently used in clin. trials, showed similar efficacy as titanocene dichloride towards the N-U 2 renal-cell carcinoma xenograft. In the heterotransplanted N-U 26 carcinoma, titanocene dichloride induced relative growth redns. by 50-56% and was similarly active as cyclophosphamide, but less effective than vinblastine applied as a single dose. Titanocene dichloride was again significantly active in the KTCTL-1M carcinoma xenograft and caused relative growth redns. by 50-65%.

In the case of the MRI-H 121 renal sarcoma xenograft, however, the organometallic compd. showed an only marginal activity which was surpassed by cyclophosphamide, vinblastine and 5-fluorouracil, all three drugs inducing significant relative growth inhibitions by 50-88%. These results confirm a significant and remarkable antitumor activity of titanocene dichloride in three out of four human renal tumors xenografted to athymic mice and suggest that clin. studies of phase ll with titanocene dichloride towards renal-cell carcinoma in human patients should be done in the near future.

Answer 41:

Bibliographic Information

Antitumor activity of SCH 66336, an orally bioavailable tricyclic inhibitor of farnesyl protein transferase, in human tumor xenograft models and wap-ras transgenic mice. Liu, Ming; Bryant, Matthew S.; Chen, Jianping; Lee, Suining; Yaremko, Bohdan; Lipari, Phil; Malkowski, Michael; Ferrari, Eric; Nielsen, Loretta; Prioli, Nicholas; Dell, Janet; Sinha, Dineshwar; Syed, Jameel; Korfmacher, Walter A.; Nomeir, Amin A.; Lin, C-C.; Wang, Lynn; Taveras, Arthur G.; Doll, Ronald J.; Njoroge, F. George; Mallams, Alan K.; Remiszewski, Stacy; Catino, Joseph J.; Girijavallabhan, Viyyoor M.; Kirschmeier, Paul; Bishop, W. Robert. Departments of Biological Research-Oncology, Schering-Plough Research Institute, Kenilworth, NJ, USA. Cancer Research (1998), 58(21), 4947-4956. Publisher: AACR Subscription Office, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 130:104933 AN 1998:728126 CAPLUS

Abstract

We have been developing a series of nonpeptidic, small mol. farnesyl protein transferase inhibitors that share a common tricyclic nucleus and compete with peptide/protein substrates for binding to farnesyl protein transferase. Here, we report on pharmacol. and in vivo studies with SCH 66336, a lead compd. in this structural class. SCH 66336 potently inhibits Ha-Ras processing in whole cells and blocks the transformed growth properties of fibroblasts and human tumor cell lines expressing activated Ki-Ras proteins. The anchorage-independent growth of many human tumor lines that lack an activated ras oncogene is also blocked by treatment with SCH 66336. In mouse, rat, and monkey systems, SCH 66336 has excellent oral bioavailability and pharmacokinetic properties. In the nude mouse, SCH 66336 demonstrated potent oral activity in a wide array of human tumor xenograft models including tumors of colon, lung, pancreas, prostate, and urinary bladder origin. Enhanced in vivo efficacy was obsd. when SCH 66336 was combined with various cytotoxic agents (cyclophosphamide, 5-fluorouracil, and vincristine). In a Ha-Ras transgenic mouse model, prophylactic treatment with SCH 66336 delayed tumor onset, reduced the av. no. of tumors/mouse, and reduced the av. tumor wt./animal. In a therapeutic mode in which gavage treatment was initiated after the transgenic mice had developed palpable tumors, significant tumor regression was induced by SCH 66336 in a dose-dependent fashion. This was assocd. with increased apoptosis and decreased DNA synthesis in tumors of animals treated with SCH 66336. Enhanced efficacy was also obsd. in this model when SCH 66336 was combined with cyclophosphamide. SCH 66336 is presently being evaluated in Phase I clin. trials.

Answer 42:

Bibliographic Information

The alkylator treosulfan shows activity towards human renal-cell carcinoma in vivo and in vitro. Koepf-Maier, P. Institut fuer Anatomie, Freie Universitaet Berlin, Berlin, Germany. In Vivo (1998), 12(3), 275-288. Publisher: International Institute of Anticancer Research, CODEN: IVIVE4 ISSN: 0258-851X. Journal written in English. CAN 129:285676 AN 1998:550055 CAPLUS

Abstract

Treosulfan (L-threitol-1,4-bismethanesulfonate, Ovastat) was tested on human renal tumor cells growing as xenografts in athymic nude mice and as monolayers in vitro, in comparison with clin. used cytostatic drugs (in vivo, cyclophosphamide, vinblastine, and 5-fluorouracil; in vitro, vinblastine and 5-fluoro-2'-deoxyuridine) which were administered at equitoxic or equiv. dose levels, resp. Four human renal tumor xenografts (N-U 2, N-U 26, MRI-H 121, KTCTL-1M) were investigated in vivo, and seven renal tumor cell lines (KTCTL-1M, KTCTL-2, KTCTL-26A, KTCTL-30, KTCTL-84, MRI-H 121, N-U 2) under in vitro conditions. The investigations of the four human renal tumor xenografts revealed that treosulfan is capable of inducing pronounced growth inhibitions ranging from 60-100% in comparison with untreated control tumors. In the xenografted renal-cell carcinoma KTCTL-1M, treosulfan administered at the highest dose level (1 × 3500 mg/kg) even effected a complete remission lasting for more than three weeks in all animals treated with this dose. It was more effective in the N-U 2 carcinoma growing in vivo than the comparative compds. cyclophosphamide and vinblastine. In the heterotransplanted renal-cell carcinoma N-U 26, treosulfan showed a similar activity as the two established cytostatic drugs tested whereas, in the renal sarcoma MRI-H 121, both cyclophosphamide and vinblastine were slightly more effective than treosulfan. In four renal-cell carcinomas growing as monolayers in vitro (KTCTL-1M, KTCTL-2, KTCTL-84, N-U 2), treosulfan induced cell growth inhibitions by about 50% at peak plasma concn. in comparison with untreated control cultures. The IC50 values ranged from 5 × 10-6 to 10-4 mol/L in all seven monolayer cultures investigated. 5-Fluoro-2'-deoxyuridine (floxuridine) was similarly active in vitro as treosulfan with respect to the molar concns.

inducing growth inhibition and to the IC50 values, whereas vinblastine was more effective than treosulfan in most of the

human renal tumor cell monolayers investigated. These results reveal the remarkable antitumor efficacy of treosulfan toward human renal-cell carcinomas, esp. under in vivo conditions. This activity was similarly high or even better than in cyclophosphamide and vinblastine. The in vitro data obtained in monolayer cultures also confirmed the remarkable antiproliferative activity of treosulfan in renal tumor cells, but did not mirror very well the pattern of antitumor activity obsd. in vivo.

Answer 43:

Bibliographic Information

Multidrug resistance genes (MRP) and MDR1 expression in small cell lung cancer xenografts: relationship with response to chemotherapy. Canitrot, Yvan; Bichat, Francis; Cole, Susan P. C.; Deeley, Roger G.; Gerlach, James H.; Bastian, Gerard; Arvelo, Francisco; Poupon, Marie-France. Cancer Research Laboratories, Queen's University, Kingston, ON, Can. Cancer Letters (Shannon, Ireland) (1998), 130(1,2), 133-141. Publisher: Elsevier Science Ireland Ltd., CODEN: CALEDQ ISSN: 0304-3835. Journal written in English. CAN 129:310474 AN 1998:497582 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Intrinsic or acquired drug resistance is a major limiting factor of the effectiveness of chemotherapy. Increased expression of either the MRP gene or the MDR1 gene has been demonstrated to confer drug resistance in vitro. In this study, we examd. MRP and MDR1 gene expression in a panel of 17 small cell lung cancers (SCLC) xenografted into nude mice from treated and untreated patients using an RT-PCR technique. For some of them, the outcome of the corresponding patients was known and we related MDR1/MRP expression with the xenograft response to C'CAV (cyclophosphamide, cisplatin, adriamycin and etoposide) combined chemotherapy. Fifteen (88%) of the 17 cases of SCLC were found to be pos. for either MDR1 or MRP. MRP gene expression was present in 12 (71%) of 17 cases, whereas MDR1 gene expression was detected in eight (50%) of 16 cases. For six SCLC, the survival duration of patients differed, with three patients surviving for >30 mo after therapy. Among these six tumors, five expressed MRP and/or MDR1. These six xenografts responded to the C'CAV treatment but a significant rate of cure was obtained in only three cases. No obvious relationship was obsd. between the response to this treatment and MRP or MDR1 expression. However, the remarkably high levels and frequency of MRP expression in some SCLC samples indicate that future developments in chemotherapy of this tumor type should anticipate that drugs which are substrates of MRP may be of limited effectiveness.

Answer 44:

Bibliographic Information

An oncolytic viral mutant that delivers the CYP2B1 transgene and augments cyclophosphamide chemotherapy. Chase, Maureen; Chung, Richard Y.; Chiocca, E. Antonio. Mol. Neuro-oncol. Lab., Neurosurgical Service, Massachusetts Gen. Hosp.-CNY6, Harvard Med. Sch., Charlestown, MA, USA. Nature Biotechnology (1998), 16(5), 444-448. Publisher: Nature America, CODEN: NABIF9 ISSN: 1087-0156. Journal written in English. CAN 129:49315 AN 1998:309047 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Herpes simplex viruses type 1 (HSV-1) with an inactivated viral ribonucleotide reductase (Hsrr, ICP6) were designed to target tumor cells with upregulated mammalian ribonucleotide reductase (mRR), an enzyme whose expression is regulated by the p16/pRB tumor suppressor pathway. A recombinant HSV-1 was generated by knock-out of Hsrr and insertion of the rat CYP2B1 transgene responsible for the bioactivation of the prodrugs, cyclophosphamide and ifosfamide. The mutant virus replicated selectively in rat and human tumor cells that express mRR. Addn. of cyclophosphamide potentiated oncolytic effects against cultured tumor cells and s.c. tumor xenografts established in athymic mice.

Answer 45:

Bibliographic Information

Prostate carcinoma response to cytotoxic therapy: in vivo resistance. Teicher, Beverly A.; Kakeji, Yoshihiko; Ara, Gulshan; Herbst, Roy S.; Northey, David. Dana-Farber Cancer Institute and Joint Center for Radiation Therapy, Boston, MA, USA. In Vivo (1997), 11(6), 453-462. Publisher: International Institute of Anticancer Research, CODEN: IVIVE4 ISSN: 0258-851X. Journal written in English. CAN 128:252636 AN 1998:145193 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Androgen independent prostate cancer is recognized as a chemotherapy resistant disease. Human prostate carcinoma DU-145, LNCaP and PC-3 cells in monolayer in exponential growth were exposed to various concns. of melphalan, 4-hydroperoxycyclophosphamide or adriamycin for 1 h. These cells were all responsive to the drugs, with DU-145 cells being the least sensitive and PC-3 cells the most sensitive. When the three human prostate carcinoma cell lines were grown as xenografts in nude or SCID mice and the animals treated with single doses of melphalan, cyclophosphamide or adriamycin, the tumors were not very responsive to the drugs. The DU-145 tumors were highly resistant to each drug. The PC-3 tumors were more sensitive; however, even the PC-3 tumors were less drug responsive than several murine tumors. All three prostate cell lines secreted transforming growth factor-β (TGF-β) into the cell culture medium, and when grown as xenograft tumors increased the plasma levels of TGF-β in the animals. DU-145 cells produced the most TGF-β and LNCaP cells produced the least. After administration of single doses of each of the chemotherapeutic agents to animals bearing the prostate carcinoma xenografts, there was a time dependent increase in plasma TGF-β that was greatest in animals bearing the DU-145 tumor and least in animals bearing the LNCaP tumor. Immunohistochem. staining, showed that PC-3 tumors tended to have the most intense staining for TGF-β and LNCaP tumors the least. In situ hybridization for TGF-β mRNA showed an increase in TGF-β mRNA that was time independent after chemotherapy administration in all three tumors. These results support the hypothesis that the drug resistance of prostate carcinoma is manifest in vivo, and that in vivo high levels of TGF-β may protect these tumors from cytotoxic cancer therapies.

Answer 46:

Bibliographic Information

Potent therapeutic activity of irinotecan (CPT-11) and its schedule dependency in medulloblastoma xenografts in nude mice. Vassal, Gilles; Boland, Isabelle; Santos, Alexandre; Bissery, Marie-Christine; Terrier-Lacombe, Marie-Jose; Morizet, Jackie; Sainte-Rose, Christian; Lellouch-Tubiana, Arielle; Kalifa, Chantal; Gouyetre, Alain. Laboratory of Pharmacotoxicology and Pharmacogenetics (CNRS URA147), Institut Gustave-Roussy, Villejuif, Fr. International Journal of Cancer (1997), 73(1), 156-163. Publisher: Wiley-Liss, CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 128:18460 AN 1997:693561 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The anti-tumor activity of irinotecan (CPT-11), a DNA-topoisomerase I inhibitor, was evaluated in 5 advanced stage s.c. medulloblastoma xenografts in nude mice, using different schedules of administration. With a 5-day schedule, the highest i.v. dose tested (40 mg kg-1 day-1) induced complete regressions in all xenografts but 1, and delays in tumor growth always exceeded 30 days. Two xenografts, IGRM11 and IGRM33, were highly sensitive, and animals survived tumor-free beyond 120 days after treatment. CPT-11 clearly retained its anti-tumor activity at a lower dosage (27 mg kg-1 day-1). CPT-11 was significantly more active than cyclophosphamide, thiotepa and etoposide against the 3 xenografts evaluated. To study the schedule dependency of its anti-tumor activity, CPT-11 was given i.v. at the same total doses over the same period (33 days) using either a protracted or a sequential schedule in IGRM34-bearing mice. With a dose of 10 mg kg-1 day-1 given on days 0-4, days 7-11, days 21-25 and days 28-32 (total dose, 200 mg kg-1), 3 of 6 animals were tumor free on day 378. The same total dose given with a sequential schedule, i.e., 20 mg kg-1 day-1 on days 0-4 and days 28-32, failed to induce complete regression. The plasma pharmacokinetics of CPT-11 and SN-38 (active metabolite of CPT-11) were studied in IGRM34-bearing animals after a single i.v. dose of 10 and 40 mg kg-1. The plasma clearance rate of CPT-11 was dose dependent. The ratio between the SN-38 and CPT-11 area under the curve in plasma was 0.4-0.65, i.e., significantly higher than that obsd. in humans at the max. tolerated dose (0.01-0.05). Conversely, this ratio was 10-fold lower in tumor than in plasma. Clin. development of irinotecan is warranted in pediatric malignancies.

Answer 47:

Bibliographic Information

Antitumor activity of menogaril alone, and in combination against human mammary cancer models in mice and rats. Yoshida, Masahiko; Fujioka, Akio; Nakano, Koushi; Kobunai, Takashi; Saito, Hitoshi; Toko, Toshiyuki; Takeda, Setsuo; Unemi, Norio. Anticancer and Antimicrobials Research Laboratory, Taiho Pharmaceutical Co., Ltd., Tokushima, Japan. Anticancer Research (1996), 16(3A), 1155-1159. Publisher: Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 125:185052 AN 1996:472482 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Menogaril is an antitumor agent different from other anthracyclines in being active after oral administration. To predict its clin. effectiveness by this route against human breast cancer, its antitumor activity was compared against breast cancer in exptl. animals with that of injected Adriamycin. Menogaril had half the much antitumor activity of Adriamycin against human mammary cancer cell lines. Menogaril given orally also had a antitumor activity against mammary cancer caused by 7,12-dimethylbenz[a]anthracene in rats comparable with that of adriamycin. The high concn. of menogaril in tumor tissue seemed to contribute to its effectiveness. Of several combinations of cyclophosphamide, Adriamycin, menogaril, and 5-fluorouracil, the combination of cyclophosphamide, menogaril, and 5-fluorouracil was most effective against mouse leukemia L1210 and human breast cancer xenografts in mice. This combination might have antitumor activity against breast cancer superior to that of the therapy currently of 1st choice (cyclophosphamide, Adriamycin, and 5-fluorouracil) in the clinic.

Answer 48:

Bibliographic Information

In vivo/in vitro correlation of xenografts in nude mice and the ATP-cell viability assay. Perras, James P.; Hurst, Josephine. School Medicine, University Miami, Miami, FL, USA. Contributions to Gynecology and Obstetrics (1994), 19(Chemosensitivity Testing in Gynecologic Malignancies and Breast Cancer), 122-131. Publisher: Karger, CODEN: CGOBD6 ISSN: 0304-4246. Journal written in English. CAN 125:131526 AN 1996:450444 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors compare in vitro results of an ATP cell viability assay (ATP-CVA) to the in vivo chemosensitivity of transplanted ovary and breast xenografts in nude mice. This approach not only allows a comparison between the in vitro and in vivo systems, but it also provides a means to compare responses using multiple tumor specimens to evaluate the reproducibility of the ATP- CVA. The results strongly indicate that the ATP-CVA in vitro chemosensitivity assay provides an approach that, to a degree, approximates a clin. situation. With this method, the initial evaluations of in vitro chemosensitivity assays can be done more quickly and easily to compare with in vivo response. It has been shown for 2 xenograft tumors (ovarian and breast) that for those drugs tested, the ATP-CVA can predict the drug sensitivity of these tumors in nude mice. The reproducibility of the ATP-CVA assay is also demonstrated.

Answer 49:

Bibliographic Information

Donor-specific prolongation of rat skin graft survival induced by rat-donor cells and cyclophosphamide under coadministration of monoclonal antibodies against T cell receptor $\alpha\beta$ and natural killer cells in mice. Umesue, Masayoshi; Mayumi, Hisanori; Nishimura, Yousuke; Kong, Young-Yun; Omoto, Kazuya; Murakami, Yoshiyuki; Nomoto, Kikuo. Medical Institute Bioregulation, Kyushu University, Fukuoka, Japan. Transplantation (1996), 61(1), 116-24. Publisher: Williams & Wilkins, CODEN: TRPLAU ISSN: 0041-1337. Journal written in English. CAN 124:219822 AN 1996:125171 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Because of the recent interest in human xenotransplantation, the authors investigated the possibility of inducing tolerance in a xenogeneic combination using cyclophosphamide (CP). Donor-specific prolongation of xenogeneic Fisher 344 (F344) rat skin graft survival for ≤60 days was induced in C57BL/6 (B6) mice by giving F344 bone marrow cells and spleen cells on day 0, CP on day 2, and monoclonal antibodies against murine TCR-αβ and NK1.1 on days -1 and 3. The inoculation of the xenogeneic cells brought accelerated repopulation of TCR-αβ+ T cells, even after the administration of anti-TCR-αβ mAb. The quick increase of the host TCR-αβ+ T cells caused by the xenogeneic cell injection was deeply suppressed by CP. Mixed lymphocyte reaction, CTL activity, and antibody prodn. against donor F344 were profoundly suppressed for 50 days. Mixed xenogeneic chimerism was obsd. for 1 mo after the inoculation of donor cells in the spleen and peripheral blood of the recipient B6 mice, but was never obsd. in the thymus. Moreover, when irradiated F344 cells were used in place of viable cells, chimerism was never detected and graft survival was only slightly prolonged. Clonal deletion of Vβ5- or Vβ11-bearing murine T cells was not obsd. on day 50 in the thymus or spleen of the recipient B6 mice. These results suggest that treatment with viable xenogeneic donor cells, CP, and mAbs against T and NK cells can induce a temporary peripheral mixed chimerism and donor-specific prolongation of xenogeneic skin graft survival. The destruction with CP of T and B cells that are xenoreactive and thus proliferating after antigen stimulation, followed by mechanisms other than intrathymic clonal deletion, may be the mechanism of the hyporesponsiveness in the present system.

Answer 50:

Bibliographic Information

Adding a reverser (verapamil) to combined chemotherapy overrides resistance in small cell lung cancer xenografts.
Arvelo, F.; Poupon, M. F.; Bichat, F.; Grossin, F.; Bourgeois, Y.; Jacrot, M.; Bastian, G.; Le Chevalier, T. CNRS, Institut Curie, Paris, Fr. European Journal of Cancer, Part A (1995), 31A(11), 1862-8. Publisher: Elsevier, CODEN: EJCTEA Journal written in English. CAN 124:134977 AN 1996:39796 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Small cell lung carcinomas (SCLC) are characterized by chemosensitivity to diverse antitumoral compds. However, responses are transitory and relapses are commonly obsd. The authors examd. the ability of verapamil, a reverser of P-glycoprotein (Pgp)-related resistance, to improve the efficacy of CyCAV combined chemotherapy (Cy, cyclophosphamide (CPA); C, cisplatin (CDDP); A, doxorubicin (ADM);V, etoposide (VP16)), as currently administered to SCLC patients at Institute Gustave-Roussy, France, and adapted to the treatment of nude mice implanted with these tumors. Although Pgp encoded by the MDR1 (multidrug resistance) gene is not the only mechanism for multidrug resistance (MDR), and not all drugs included in this regimen are recognized by Pgp, the authors anticipated a therapeutic benefit. Four different SCLC lines, expressing the MDR1 gene and recently grafted into nude mice, were used. SCLC-75, SCLC-6 and SCLC-41 originated from untreated patients, and SCLC-74T was derived from a patient treated with a combination of ADM, CPA and VP16. SCLC-41T and SCLC-6T tumors were used after having undergone, resp., five and nine cycles of in vivo passage and CyCAV treatment of the tumor-bearing nude mice, to reinforce their chemoresistance. The efficacy of the CyCAV regimen, assocd. with or without verapamil (given 24 h before CyCAV on days 1-5), was tested on the growth of these SCLC. Verapamil (25 mg/kg) improved the antitumor effect of CyCAV in mice bearing SCLC-6T, SCLC-41T and SCLC-75 tumors, although toxicity was obsd. Verapamil modestly delayed the plasma clearance of ADM. Two daily injections of 10 mg/kg of verapamil, administered at a 3 h interval, proved to be effective, whereas the same total dose administered as a bolus was not. These results indicate that the assocn. of some reversers of MDR, including drugs possibly interacting with Pgp, might potentiate SCLC combined chemotherapy.

Answer 51:

Bibliographic Information

The induction of skin xenograft tolerance in rat-to-mouse combination could be affected by DFR mediating cells and antibodies against rat bone marrow cells as well as NK cells in the cyclophosphamide-induced tolerance system.
Nishimura, Yousuke; Eto, Masatoshi; Maeda, Takeshi; Hiromatsu, Kenji; Nomoto, Kenichi; Kong, Young-Yun; Nomoto, Kikuo. Faculty of Medicine, Kyushu University, Fukuoka, Japan. Immunobiology (Stuttgart) (1995), 193(5), 420-38. Publisher: Fischer,

CODEN: IMMND4 ISSN: 0171-2985. Journal written in English. CAN 123:283532 AN 1995:853546 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors investigated whether the prolongation of skin xenograft survival was obtained by a tolerance-inducing method using cyclophosphamide (CY), by which long-lasting skin allograft tolerance could be induced. The long-lasting skin allograft survival could be obtained in the recipient C3H/HeN (C3H) mice which were given 100 μg of anti-CD4 mAb on day -3, 1×108 spleen cells (SC) plus 3×107 bone marrow cells (BMC) derived from C57BL/6 (B6) mice on day -2, 200 mg/kg CY on day 0, and which were grafted with allogeneic B6 skin on day 14. When the C3H mice were treated with anti-CD4 mAb, 1×108 SC plus 5×107 BMC derived from F344 rat and CY, the F344 skin grafts survived slightly longer (about 15 days) than those in untreated recipients (about 8.4 days). Such a prolongation of skin xenograft survival was considered donor-specific because rejection of 3rd party skin grafts from BN rats occurred significantly earlier than that of F344 skin grafts. In the recipient C3H mice treated with anti-CD4 mAb, F344 SC plus BMC and CY, mixed chimerism in the periphery was detected for a few days after CY administration, although intrathymic chimerism was not detected throughout this study. In these recipient C3H mice, cytotoxic T lymphocytes (CTL) against F344 antigens were completely abrogated though the delayed footpad reaction (DFR).

Answer 52:

Bibliographic Information

Flunarizine enhancement of melphalan activity against drug-sensitive/resistant rhabdomyosarcoma. Castellino, SM; Friedman, HS; Elion, GB; Ong, ET; Marcelli, SL; Page, R; Bigner, DD; Dewhirst, MW. Medical Center, Duke University, Durham, NC, USA. British Journal of Cancer (1995), 71(6), 1181-7. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 123:132165 AN 1995:674432 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Flunarizine was tested for its ability to modulate either cyclophosphamide- or melphalan-induced growth delay of a drug-resistant rhabdomyosarcoma xenograft (TE-671 MR) in nude mice and the drug-sensitive parent line (TE-671), in which P-glycoprotein is not involved in the mechanism of drug resistance. Tumor blood flow was increased by 30% after a flunarizine dose of 4 mg/kg, but no modification in growth delay was induced by melphalan (12 mg/kg). In contrast, a 60-mg/kg dose of flunarizine had no effect on tumor blood flow, but the same dose enhanced melphalan-induced tumor regrowth delay in both tumor lines. The dose-modifying factor for flunarizine as an adjuvant to melphalan was approx. 2 for both tumor lines. Although blood flow measurements were not performed with the combination of flunarizine and melphalan, the results with flunarizine alone suggested that the augmentation of melphalan cytotoxicity is not mediated by changes in blood flow. In contrast, flunarizine did not affect drug sensitivity to cyclophosphamide in animals bearing the drug-sensitive parent tumor line. These results suggest that the mechanism of drug sensitivity modification by flunarizine is not related to modification of tumor blood flow, but may be mediated by modification of transport mechanisms that are differentially responsible for cellular uptake and retention of melphalan as compared with cyclophosphamide.

Answer 53:

Bibliographic Information

Predictability of clinical response to anticancer agents in human cancer xenografts. Tsukamoto, Fumine. Med. Sch., Osaka Univ., Suita, Japan. Osaka Daigaku Igaku Zasshi (1994), 46(4), 251-61. CODEN: ODIZAK ISSN: 0369-710X. Journal written in Japanese. CAN 121:124753 AN 1994:524753 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mouse transplanted human tumors retained original sensitivity to antitumor drugs, and was useful in secondary screening for the

sensitivity to tumor chemotherapy. Fresh tumor tissues were transplanted and maintained in nude mice in 77 cases (tried: 247 cases), and sensitivity of the transplanted tumors to chemotherapy was compared between human therapy and in nude mice using regimen used clin. in 17 cases with 21 expts. (stomach, breast, colon, pancreas, esophagus. melanoma). Tested drugs were adriamycin, cisplatin, cyclophosphamide, cytarabine, dacarbazine, doxifluoridine, epirubicin, 5-fluorouracil, M-83 (a mitomycin C deriv.), mitomycin C, tegafur, and UFT. Chemotherapy in nude mice was effective in 6 expts., which coincided with clin. results in 5 cases. The ineffective 15 cases in nude mice coincided with the clin. results in all cases.

Answer 54:

Bibliographic Information

Synergistic interaction between tirapazamine and cyclophosphamide in human breast cancer xenografts. Langmuir, Virginia K.; Rooker, Julie A.; Osen, Maureen; Mendonca, Holly L.; Laderoute, Keith R. SRI Int., Menlo Park, CA, USA. Cancer Research (1994), 54(11), 2845-7. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 121:415 AN 1994:400415 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study examd. the efficacy of combining cyclophosphamide and the hypoxic cytotoxin, tirapazamine, in the treatment of human breast cancer xenografts grown in nude mice. A single dose of tirapazamine was followed 2 h later by a single dose of cyclophosphamide. As detd. from tumor regrowth delay, the effectiveness of combined therapy was greater than the additive effects of each treatment given alone. Possible mechanisms of this synergistic interaction include enhancement of DNA damage, inhibition of repair of DNA damage, or induction of apoptosis. Apart from some loss in body wt., the only other toxicity of interest in mice treated with tirapazamine was necrosis of the skin on the distal tail, which appeared to be vascular in origin.

Answer 55:

Bibliographic Information

Local hyperthermia enhances cyclophosphamide, ifosfamide and cis-diamminedichloroplatinum cytotoxicity on human-derived breast carcinoma and sarcoma xenografts in nude mice. Wiedemann, Guenter; Roszinski, Stefan; Biersack, Anke; Weiss, Christoph; Wagner, Thomas. Dep. Intern. Med., Med. Univ. Luebeck, Luebeck, Germany. Journal of Cancer Research and Clinical Oncology (1992), 118(2), 129-35. CODEN: JCROD7 ISSN: 0171-5216. Journal written in English. CAN 120:153172 AN 1994:153172 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Antitumor response and toxicity of locally applied hyperthermia with or without cyclophosphamide, ifosfamide, and cis-diamminedichloroplatinum (cisplatin) have been compared. The model systems were human breast carcinoma (MX1/3) and human sarcoma (S117) grown in nude mice. To detect changes of tumor oxygenation, intratumoral PO2 and pH were measured before, during and following hyperthermia. In both human tumor lines, a monotherapy with one of the cytotoxic drugs or with hyperthermia caused a transient growth delay, while the combination of the same dose of the drugs with hyperthermia (at 43° for 1 h) resulted in complete tumor remissions. During hyperthermia, in both tumor types, oxygenation was improved. Intratumoral pH remained practically unchanged.

Answer 56:

Bibliographic Information

Comparison of iodine-131-labeled antiepisialin 139H2 with cisplatin, cyclophosphamide or external-beam radiation for antitumor efficacy in human ovarian cancer xenografts. Molthoff, Carla F. M.; Pinedo, Herbert M.; Schluper, Hennie M. M.;

Rutgers, Derk H.; Boven, Epie. Dep. Oncol., Free Univ. Hosp., Amsterdam, Neth. International Journal of Cancer (1992), 51(1), 108-15. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 117:3422 AN 1992:403422 CAPLUS

Abstract

Three human ovarian cancer xenografts of different origin and grown s.c. in nude mice as well-established tumors were studied for their sensitivity to cisplatin (CDDP), cyclophosphamide (CTX), 131I-labeled antiepisialin monoclonal antibody (MAb) 139H2, or external-beam radiotherapy. The max. tolerated dose of CDDP given weekly i.v. × 2 induced a tumor growth inhibition (GI) of 77.5% and 85.1% of the serous xenografts Ov.Ri(C) and OVCAR-3, resp. The mucinous xenograft Ov.Pe was relatively resistant to CDDP. The max. tolerated dose of CTX, given i.p. × 2 with a 2-wk interval, induced a GI between 52.9% and 59.7% for each of the 3 xenografts. Radioimmunotherapy with 500-750 μCi 131I-specific MAb 139H2, administered i.v. × 2 with a 2-wk interval, was more effective than CDDP or CTX. The 500 μCi 131I-MAb 139H2 schedule induced 100% GI in Ov.Ri(C) xenografts and all tumors were cured. The same schedule was slightly less effective in OVCAR-3 xenografts, but complete tumor regressions could still be obtained. Ov.Pe xenografts were least sensitive to radioimmunotherapy. The 2 injections of 500 μCi 131I-control MAb gave only transient growth inhibition of OVCAR-3 and Ov.Pe tumors, but gave complete regressions of Ov.Ri(C) xenografts. Biodistribution using tracer doses of 131I-MAb 139H2 and 125I-control MAb showed different degrees of specificity for MAb 139H2 in the 3 xenografts. Radiation doses absorbed in OV.Ri(C), OVCAR-3 and Ov.Pe xenografts per 10 μCi injected dose were 30, 41 and 29 cGy resp. Treatment with 10 Gy external-beam radiation suggests that the effects of radioimmunotherapy in each tumor line were related to the intrinsic radiosensitivity of the xenografts.

Answer 57:

Bibliographic Information

Studies on chemotherapy for adenocarcinoma of the uterine cervix using xenografts transplanted in nude mice. Yamagishi, Masaji. Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1991), 43(2), 165-72. CODEN: NISFAY ISSN: 0300-9165. Journal written in Japanese. CAN 115:341 AN 1991:400341 CAPLUS

Abstract

Adenocarcinoma of the human uterine cervix was successively transplanted into nude mice and the effects of chemotherapy on adenocarcinoma of uterine cervix were investigated in this transplanted tumor. First, it was confirmed that both the original tumor and the transplanted tumor were apparently histol. the same as adenocarcinoma of the uterine cervix (endocervical type). And the transplanted tumor was shown to have the features of adenocarcinoma by an electron microscope. The doubleing time of the transplanted tumor was 9.2 days. For the chemotherapy study, first the therapeutic effects of 11 kinds of agents were screened by single-agent chemotherapy applied to the transplanted tumor. From the results of this series, 6 regimens for multi-agent chemotherapy were tried on the transplanted tumor. The effects of the chemotherapy were evaluated following Battelle Columbus Labs. Protocol and histopathol. The relative regression rates for the tumors treated with mitomycin C (MMC) + cyclophosphamide (CPM) and MMC + CPM + methotrexate (MTX) were 72.99 and 80.9% (Tn/To = 0.84), resp. The results suggest that the combinations of MMC + CPM or MMC + CPM + MTX are regimens that are possibly effective on the adenocarcinoma of human uterine cervix and are worth be trying clin.

Answer 58:

Bibliographic Information

Antitumor effects of cisplatin, cyclophosphamide, and interferon-γ (γ-IFN) against argyrophil small cell carcinoma of the uterine cervix heterotransplanted into nude mice. Shimizu, Hiromu; Yamasaki, Masato; Ichimura, Hiroshi; Kurimura, Osamu. Dep. Obstet. Gynecol., Kure Natl. Hosp., Hiroshima, Japan. Gan to Kagaku Ryoho (1989), 16(12), 3777-80. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 112:171897 AN 1990:171897 CAPLUS

Abstract

The antitumor effect of cis-diammine-dichloroplatinium (cisplatin or CDDP), cyclophosphamide (CY), and interferon-γ (γ-IFN) against argyrophil small cell carcinoma (ASCC) of the uterine cervix was studied using heterotransplanted ASCC tumor (YIK-1) into nude mice, contg. HPV 16 DNA in a multicopy integrated form. No tumor growth retardation was obsd. in the nude mice which received the single administration of CDDP 2 mg/kg, CY 10 mg/kg or γ-IFN 1 × 107 U/kg. However, the combined administration of CDDP and CY, or CDDP, CY and γ-IFN markedly inhibited the tumor growth. Moreover, with comparison about relative tumor vol. between these two groups, the combination of CDDP, CY and γ-IFN was more effective than that of CDDP and CY. These data suggest that the combination chemotherapy of CDDP, CY, and/or γ-IFN was effective for the suppression of tumor growth in argyrophil small cell carcinoma of the uterine cervix.

Answer 59:

Bibliographic Information

Experimental chemotherapy of human medulloblastoma cell lines and transplantable xenografts with bifunctional alkylating agents. Friedman, Henry S.; Colvin, O. Michael; Skapek, Stephen X.; Ludeman, Susan M.; Elion, Gertrude B.; Schold, S. Clifford, Jr.; Jacobsen, Phillip F.; Muhlbaier, Lawrence H.; Bigner, Darell D. Med. Cent., Duke Univ., Durham, NC, USA. Cancer Research (1988), 48(15), 4189-95. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 109:142110 AN 1988:542110 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A series of bifunctional alkylators were tested against the genotypically and phenotypically heterogeneous continuous human medulloblastoma cell lines TE-671, Daoy, and D283 Med in vitro and against TE-671 and Daoy growing as s.c. and intracranial xenografts in athymic mice. Drugs tested included melphalan, cyclophosphamide, iphosphamide, phenylketocyclophosphamide, thiotepa, 1,3-bis(2-chloroethyl)-1-nitrosourea (in vivo), and busulfan (in vivo). Melphalan and phenylketocyclophosphamide were the most active agents in vitro, with drug concns. at which there is a 90% redn. in the no. of colonies of 2.13, 5.29, and 4.72 μM for melphalan and 4.60, 5.01, and 4.34 μM for phenylketocyclophosphamide against TE-671, D283 Med, and Daoy, resp. Melphalan, cyclophosphamide, iphosphamide, phenylketocyclophosphamide, and thiotepa produced significant growth delays against s.c. TE-671 and Daoy xenografts, while no activity could be demonstrated for 1,3-bis(2-chloroethyl)-1-nitrosourea or busulfan. Melphalan, cyclophosphamide, iphosphamide, and thiotepa also produced significant increases in median survival in mice bearing intracranial TE-671 and Daoy xenografts. These results extend previous studies demonstrating the antitumor activity of N- and phosphoramide mustard-based bifunctional alkylating agents in the treatment of human medulloblastoma continuous cell lines and transplantable xenografts, and support the continued use of these agents in clin. trials.

Answer 60:

Bibliographic Information

Fundamental study of 6-day subrenal capsule assay by cyclophosphamide pretreatment. Terashima, Masanori; Ikeda, Kenichiroh; Kawamura, Shuji; Satoh, Masao; Ishida, Kaoru; Amano, Kazuyuki; Takagane, Akinori; Yaegashi, Yasunori; Saitoh, Kazuyoshi. 1st Dep. Surg., Iwate Med. Univ., Japan. Gan to Kagaku Ryoho (1988), 15(3), 505-11. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 109:16730 AN 1988:416730 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Immunosuppression with cyclophosphamide prior to the evaluation of the antitumor activity of chemotherapeutic agents against transplanted human esophageal cancer xenograft in the subrenal capsule assay in mice resulted in activities similar to those seen with the drugs in a nude mouse assay system. Increases in toxicity in the cyclophosphamide-pretreated animals was small.

Answer 61:

Bibliographic Information

Effect of immunosuppressants on subrenal capsule (SRC) assay as a chemosensitivity test. Irimajiri, Nobuhiro; Haneda, Junichi; Yokoyama, Eiji; Shirakabe, Masaya; Matsumoto, Masamichi; Kusunoki, Tokuro; Utsunomiya, Joji. 2nd Dep. Surg., Hyogo Med. Coll., Nishinomiya, Japan. Gan to Kagaku Ryoho (1988), 15(3), 449-55. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 109:16729 AN 1988:416729 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Six-day SRC assay as a chemosensitivity test has an advantage of high predictive rate for clin. response. However, very few viable tumor cells are obsd. at the end of the assay, making the assay results unreliable. The effect of immunosuppressants on the SRC assay was tested with Walker carcinosarcoma from Wistar rat xenografted under the renal capsule of BDF1 mice. The changes of tumor size, pathol. features and proliferative ability of the tumor xenografted under the renal capsule of mice treated with cyclophosphamide, mizolibine or cyclosporin A were examd. Only cyclosporin A treatment maintained the viable tumor cells and proliferative ability of the tumor grafted under the renal capsule 21 days after transplantation. In order to compare the original 6-day SRC assay developed by Bogden et al., immunosuppressants were applied to the 6-day assay. The results suggested that cyclosporin A and mizolibine increase tumor sensitivity in 6-day SRC assay.

Answer 62:

Bibliographic Information

Combination chemotherapy with three or four drugs on human breast and gastrointestinal cancer xenografts in nude mice (II). Fujita, Fumiko; Fujita, Masahide; Sakamoto, Yasuo; Shimozuma, Kojiro; Inaba, Hiizu; Taguchi, Tetsuo. Res. Inst. Microb., Osaka Univ., Osaka, Japan. Gan to Kagaku Ryoho (1987), 14(5, Pt. 1), 1252-9. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 107:126597 AN 1987:526597 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Combined applications of 4 drugs, vindesine (VDS), methotrexate (MTX), cisplatin (CDDP) and 5'-DFUR (5'-deoxy-5-fluorouridine) against 3 lines of human breast cancer (H-62, H-31, H-71), and one line each of gastric cancer (H-55) and colon cancer (H-110) xenografted into nude mice were evaluated in comparison with CAF (cyclophosphamide, adriamycin and 5-fluorouracil (5-FU) therapy which is commonly used for breast cancer. Combination therapy with 3 drugs (VDS, CDDP and 5'-DFUR) or 4 drugs (VDS, CDP, MTX and 5'-DFUR) achieved a marked effect with tumor shrinkage in 3 lines of tumors (H-55, H-31 and H-62). Moreover, remarkable effects were shown even in the other 2 lines which were insensitive to every single-agent therapy. A synergistic effect was obtained in 3 of the 5 lines examd. These combination therapies were histol. superior to therapies employing single-drug or CAF therapy. The side effects for combination of these 3 or 4 drugs evaluated by body wt. loss were transient and equiv. to maximal dose of VDS or CDCP.

Answer 63:

Bibliographic Information

Sensitivity of human non-small cell lung cancer xenografts to cyclophosphamide and cisplatin. Mattern, J.; Wayss, K.; Volm, M. Inst. Exp. Pathol., Ger. Cancer Res. Cent., Heidelberg, Fed. Rep. Ger. In Vivo (1987), 1(1), 23-6. CODEN: IVIVE4 ISSN: 0258-851X. Journal written in English. CAN 107:126374 AN 1987:526374 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of cyclophosphamide and cisplatin was tested against 14 human non-small cell lung tumor xenografts in nude mice. The previously reported poor clin. response of non-small cell tumors to these 2 drugs paralleled the lack of response of the xenografts. Thus, the nude mouse xenograft system may be used as a predictive screen for antineoplastic agents.

Answer 64:

Bibliographic Information

Chemo-sensitive differences of primary, metastatic and recurrent tumors of human colorectal cancer. Yamada, Kazutaka; Takao, Sonshin; Maenohara, Shigeho; Saihara, Tetushi; Yoshinaga, Atsunori; Haruyama, Katsuro; Mitsuda, Kazunobu; Makizumi, Kanro; Ishizawa, Takashi; Shimazu, Hisaaki. Sch. Med., Kagoshima Univ., Kagoshima, Japan. Nippon Shokakibyo Gakkai Zasshi (1986), 83(11), 2318-24. CODEN: NIPAA4 ISSN: 0369-4259. Journal written in Japanese. CAN 106:207311 AN 1987:207311 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Tumor lines xenografts in nude mice used in this study include COK-1 and COK-7. COK-1 (PT, LN and RE) has been established from the primary (PT) lymph node metastatic (LN) and local recurrent (RE) tumors of human colon cancer, and COK-7 (PT and LiM) has been established from the primary(PT) and liver metastatic(LiM) tumors of human rectal cancer. These tumor lines were used for the study of chemotherapeutic responses to such anti-cancer drugs as 5-fluorouracil [51-21-8], cyclophosphamide [50-18-0], cisplatin [15663-27-1], and mitomycin C (MMC) [50-07-7]. Chemotherapeutic responses to these drugs in each tumor line were as follows: COK-1 (PT) responded to only MMC, while COK-1 (RE) responded to both MMC and cisplatin. However, COK-1 (LN) did not respond to any drug studied. In case of COK-7 (PT) it did not respond to drug as well, though COK-7 (LiM) showed a response to MMC. These results indicate that each tumor line of COK-1 and COK-7 has chemosensitive differences in primary, metastatic, and recurrent tumor lines.

Answer 65:

Bibliographic Information

AUC-dependent cytotoxicity of cyclophosphamide against human tumors transplanted into nude mice. Sugiyama, Masatoshi; Okamura, Kentarou; Goto, Mitsuyoshi; Kitano, Morihisa. Dep. Pharm., Fukui Med. Sch. Hosp., Fukui, Japan. Journal of Clinical Biochemistry and Nutrition (1986), 1(2), 171-9. CODEN: JCBNER ISSN: 0912-0009. Journal written in English. CAN 106:78344 AN 1987:78344 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The cytotoxicity of cyclophosphamide [50-18-0] following the administration of phenobarbital [50-06-6] or chloral hydrate [302-17-0] to nude mice bearing human tumor xenografts was studied. Cyclophosphamide, 60 mg/kg, was injected i.p. once a week for four weeks. The antitumor efficacy of cyclophosphamide was not altered by pretreatment with phenobarbital, but was significantly increased by pretreatment with chloral hydrate. In a parallel study, the concn. of blood (nitrobenzyl)pyridine [1083-48-3]-alkylating metabolites in nude mice after administration of cyclophosphamide 60 mg/kg was measured. The AUC (area under blood decay curve) values of (nitrobenzyl)pyridine-alkylating metabolites were 299, 270, and 521 nmol eq nor-mustard mL-1·h in controls, phenobarbital-pretreated, and chloral hydrate-pretreated groups, resp. In contrast, Cmax (maximal concn.) values did not show any significant differences among these 3 groups. An increase in the AUC value of (nitrobenzyl)pyridine-alkylating metabolites might have led to the stimulation of cytotoxicity of cyclophosphamide in the chloral hydrate-pretreated group. These results indicate that cyclophosphamide possesses AUC-dependent cytotoxicity against human tumor.

Answer 66:

Bibliographic Information

Enhanced transplantability of human ovarian cancer lines in cyclophosphamide-pretreated nude mice. Nauta, M. M.; Boven, E.; Schlueper, H. M. M.; Erkelens, C. A. M.; Pinedo, H. M. Dep. Oncol., Free Univ., Amsterdam, Neth. British Journal of Cancer (1986), 54(2), 331-5. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 105:113448 AN 1986:513448 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cyclophosphamide (CY) pretreatment of nude mice increased the transplantability of 4 out of 7 human ovarian cancer lines. Cy suppressed natural killer (NK) cell activity in nude mice, thus strongly suggesting that some human ovarian cancer xenografts are susceptible to NK cell-mediated cytotoxicity.

Answer 67:

Bibliographic Information

Experimental and clinical studies on sensitivity test of anticancer agents by 3H-thymidine autoradiography using human malignant tumor transplanted in nude mice. Nishimawari, Kazuharu. Res. Inst. Nuclear Med. Biol., Hiroshima Univ., Hiroshima, Japan. Nippon Geka Gakkai Zasshi (1986), 87(2), 141-53. CODEN: NGGZAK ISSN: 0301-4894. Journal written in Japanese. CAN 105:107845 AN 1986:507845 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The 3H-labeled thymidine [50-89-5] uptake of human xenografts transplanted in nude mice and treated with various anticancer agents was studied by autoradiog. and compared with the histol. changes on the same specimen. Human malignant tumors were transplanted into nude mice and treated with i.p. administration of Mitomycin C (MMC) [50-07-7] 5-Fluorouracil (5-FU) [51-21-8] and Cyclophosphamide (CPM) [50-18-0]. The rate of pos. sensitivity was 65.5% in MMC, 34.9% in 5-FU and 51.8% in CPM by autoradiog. evaluation, while by histol. evaluation 18.9, 14.6, and 16.9%, resp. Apparently, the autoradiog. evaluation of the tumor sensitivity to anticancer agents is more sensitive than the histol. evaluation. As to MMC and CPM, significant correlations were demonstrated between the results of this method and those of the exptl. chemotherapy in accordance with the Battelle Columbus Labs. Protocol using human malignant tumors serially transplanted into nude mice.

Answer 68:

Bibliographic Information

Pharmacokinetics of "activated" cyclophosphamide and therapeutic efficacies. Voelcker, Georg; Wagner, Thomas; Wientzek, Carla; Hohorst, Hans Juergen. Gustav-Embden-Zent. Biol. Chem., Johann Wolfgang Goeth-Univ., Frankfurt/Main, Fed. Rep. Ger. Cancer (New York, NY, United States) (1984), 54(6, Suppl.), 1179-86. CODEN: CANCAR ISSN: 0008-543X. Journal written in English. CAN 104:199727 AN 1986:199727 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In order to examine whether the different pharmacokinetic behaviors might account, at least in part, for the known differences of antitumor activity and toxicity of cyclophosphamide (CP) [50-18-0] between humans and lab. animals, the authors studied the influence of the pharmacokinetics of activated CP (4-hydroxy cyclophosphamide (C4-OH-CP) [40277-05-2]) on the therapeutic efficacy and toxicity after injection of 4-(S-ethanol)sulfidocyclophosphamide (P1) [65882-95-3], a pro drug of activated CP, into nude mice bearing heterotransplanted human bladder sarcoma. P1 was hydrolyzed in blood to yield 4-OH-CP, yielding different blood levels; these could be established either by single bolus injection of P1 or by repetitive injection of a loading dose followed by several maintenance doses which caused nearly const. levels of activated CP for a longer time period. 4-OH-CP showed more therapeutic efficacy when present in blood at relatively low levels for longer times than after bolus injection of the same dose resulting in a sharp peak level of activated CP. After a single i.p. injection of 300 mg/kg P1, which caused a bioavailability of 36 μmol/mL/min, a 67%

inhibition of tumor growth was achieved; whereas, a tumor growth redn. of 83% was obtained after injection of the same dose in 6 fractions resulting in const. blood levels with a bioavailability of only 17 μmol/mL/min. In contrast to the significant influence on antitumor efficacy of activated CP, practically no effect of pharmacokinetics on toxicity of 4-OH-CP could be obsd. Therefore, the bioavailability of activated CP, which killed 50% of the animals, was detd. to be approx. 89 μmol/mL/min after adjustment of pharmacokinetics to yield const. levels and approx. 79 μmol/mL/min after single bolus injection. The expts. presented show that by adjustment of the pharmacokinetics, the therapeutic index of P1, defined as bioavailability causing 50% of animals to die, referred to bioavailability causing 90% tumor growth inhibition, could be more than doubled.

Answer 69:

Bibliographic Information

Enhanced success rate of transplantation with human tumors in cyclophosphamide-treated nude mice. Braakhuis, Boudewijn J. M.; Nauta, Maria M.; Romijn, Johannes C.; Rutgers, Derk H.; Smink, Truus. Dep. Otolaryngol., Free Univ. Hosp., Amsterdam, Neth. JNCI, Journal of the National Cancer Institute (1986), 76(2), 241-5. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 104:122790 AN 1986:122790 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mice were injected with cyclophosphamide (CY) [50-18-0] (100 mg/kg, i.p.) prior to s.c. implantation of tumor fragments obtained from established xenograft lines or from patients. In 3 out 8 ovarian adenocarcinoma tumor lines, with a take of ≤50% in untreated control animals, tumor take was significantly increased by CY treatment to 75-100%. No effect of CY treatment on tumor take was seen with squamous cell carcinoma of the head and neck region and with lung and prostatic carcinomas. The growth rate of these xenografts was not affected by CY pretreatment. Immunol. mechanisms appear to play a role in the inhibition of tumor growth in nude mice. CY pretreatment may enhance the success rate of transplantation, but this effect appears to be limited to certain tumors.

Answer 70:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chiodetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 104:81665 AN 1986:81665 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A human tumor xenograft model using pharmacol. immunosuppressed mice was assessed for its suitability to test preclinically the sensitivity of colorectal carcinomas, bone sarcomas and melanomas against anticancer agents. Beside ionizing radiation, 14 cytotoxic drugs including 5-fluorouracil (5-FU) [51-21-8], dimethylmyleran (DMM) [55-93-6], cytosine arabinoside [147-94-4], cyclophosphamide [50-18-0], melphalan [148-82-3], mitomycin C [50-07-7], adriamycin [23214-92-8], bleomycin [11056-06-7], etoposide [33419-42-0], vinblastine [865-21-4], cisplatin [15663-27-1], procarbazine [671-16-9], DTIC [4342-03-4], and BCNU [154-93-8] were assayed. Ionizing radiation, 5-FU and DMM were also applied at LDs followed by bone-marrow rescue high-dose therapy. Four colon carcinomas responded poorly to most of the agents but one tumor displayed marked sensitivity to BCNU. LDs of radiation, 5-FU and DMM and cyclophosphamide and by an osteosarcoma to the latter drug. No strong effects were seen against melanomas. LDs of DMM induced the best regression of one colon carcinoma. In general, the superiority of high-dose therapy for solid human tumors compared to maximally tolerated doses was demonstrated. Individual carcinomas of the same type displayed different drug sensitivity.

Answer 71:

Bibliographic Information

Experimental chemotherapy of human carcinomas serially transplanted into nude mice. Kubota, Tetsuro; Asanuma, F.; Tsuyuki, K.; Kurihara, H.; Inada, T.; Ishibiki, K.; Abe, O. Dep. Surg., Keio Univ., Tokyo, Japan. Editor(s): Spitzy, K. H.; Karrer, K. Proc. Int. Congr. Chemother., 13th (1983), 18 291/55-291/59. Publisher: Verlag H. Egermann, Vienna, Austria CODEN: 53XPA8 Conference written in English. CAN 104:14592 AN 1986:14592 CAPLUS

Abstract

In nude mice transplanted with human carcinomas, most gastrointestinal carcinomas were suppressed by mitomycin C [50-07-7] and were insensitive to cyclophosphamide (CPA) [50-18-0], whereas 2 breast carcinomas and 1 hemangiosarcoma were markedly suppressed by CPA, suggesting that the chemosensitivities of these tumors were different. No differences were found in chemosensitivity between the gastric and colon carcinomas. No correlations were obsd. between the histol. differentiations of the carcinomas and the chemosensitivity to mitomycin C, adriamycin [23214-92-8], aclarubicin [57576-44-0], and CPA. However, the growth-rate of the tumors correlated with the chemosensitivity to mitomycin C and aclarubicin, i.e., the rapid-growing tumors were more sensitive than the slow-growing tumors to the drugs.

Answer 72:

Bibliographic Information

Optimum time sequence for the administration of cyclophosphamide and other drugs in vivo. Mattern, Juergen; Wauss, Klaus; Volm, Manfred. Dep. Exp. Pathol., Ger. Cancer Res. Cent., Heidelberg, Fed. Rep. Ger. Anticancer Research (1985), 5(2), 173-8. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 103:81357 AN 1985:481357 CAPLUS

Abstract

The significance of time interval for administration of a 2nd drug after a 1st dose of cyclophosphamide (CTX) [50-18-0] was studied for human ovarian, lung, and colon carcinoma lines, growing as xenografts in nude mice. The effects of combinations of 2 drugs were dependent on the interval between the administration of each drug. The most effective chemotherapy schedules were those in which adriamycin [23214-92-8] or CTX was sequenced to coincide with the time when the tumor was regrowing after a single dose of CTX. The variation of the cell kinetic parameters, as estd. by flow cytometry anal., could not be correlated with the antitumor action of the drug combination.

Answer 73:

Bibliographic Information

Differential characteristics of two newly established human breast carcinoma cell lines. Chu, Ming Y.; Hagerty, Matthew G.; Wiemann, Michael C.; Tibbetts, Lance M.; Sato, Seiji; Cummings, Frank J.; Bogaars, Hendrik A.; Leduc, Elizabeth H.; Calabresi, Paul. Dep. Med., Roger Williams Gen. Hosp., Providence, RI, USA. Cancer Research (1985), 45(3), 1357-66. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 102:129730 AN 1985:129730 CAPLUS

Abstract

Two human breast carcinoma cell lines, EP and MW, were established in culture from malignant pleural effusions. In addn. to producing tumors in antithymocyte serum-immunosuppressed mice, both cell lines showed epithelial characteristics and anchorage-independent growth in soft agar. EP and MW differed in morphol. (spindle-shaped vs. round), chromosomal mode (hyperdiploid vs. near triploid), estrogen receptor content (43.8 vs. 5.1 fmol/mg protein), cloning efficiency (0.24 vs. 15%), and activities (milliunits/106 cells) of creatine phosphokinase (25.7 vs. 62.6) and lactate dehydrogenase (346.7 vs. 778.5). Electron microscopy revealed that MW cells had more perinuclear filamentous material and more frequent intracytoplasmic vacuole formation

than did EP cells. While having no effect on MW cells at the concns. studied (10-5 to 10-11 M), β-estradiol (10-7 M) stimulated the growth of EP cells by 106% over the hormone-depleted control. In a variety of systems, EP was consistently the more drug-sensitive of the 2 lines. In vitro, EP was significantly more sensitive to methotrexate, vincristine, and 5-fluorouracil, resp. In antithymocyte serum-mouse xenografts, EP displayed a greater response to 3 different dosages of a combination of cyclophosphamide, methotrexate, and 5-fluorouracil. One such dosage (cyclophosphamide, 32.0 mg/kg/day; methotrexate, 13.0 mg/kg/day; 5-fluorouracil, 190.0 mg/kg/day; for 1 day) reduced EP and MW tumor wts. to 5.9 and 41% of controls, resp. These results correlated well with the clin. responses.

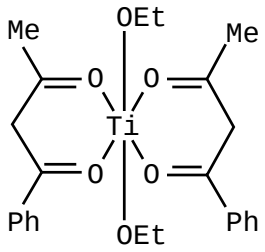
Answer 74:

Bibliographic Information

Preclinical evaluation of diethoxy(1-phenyl-1,3-butanedionato)titanium(IV) in human tumor xenografts. Mattern, J.; Keppler, B.; Volm, M. Inst. Exp. Pathol., Dtsch. Krebsforschungszent., Heidelberg, Fed. Rep. Ger. Arzneimittel-Forschung (1984), 34(10), 1289-90. CODEN: ARZNAD ISSN: 0004-4172. Journal written in English. CAN 102:55764 AN 1985:55764 CAPLUS

Abstract

The antitumor activity of diethoxy(1-phenyl-1,3-butanedionato)titanium(IV) (I) [85969-07-9] in comparison to cisplatin (cis-DDP) [15663-27-1] and cyclophosphamide (CTX) [50-18-0] against human breast, colorectal, and lung tumor lines growing as xenografts in nude mice was investigated. The antitumor activities and toxicities of I and cis-DDP were comparable, whereas CTX was the most effective agent.



I

Answer 75:

Bibliographic Information

Anticancer drug sensitivity tests using nude mice. Noso, Yoshihiro; Yoshinaka, Ken; Nishimawari, Kazaharu; Hirono, Masashi; Tani, Tadanori; Niimoto, Minoru; Hattori, Takao. Hiroshima Univ., Hiroshima, Japan. Gan no Rinsho (1984), 30(9), 1181-5. CODEN: GANRAE ISSN: 0021-4949. Journal written in Japanese. CAN 102:17009 AN 1985:17009 CAPLUS

Abstract

Both isotope assay and histol. methods were found useful for the screening of neoplasm inhibitors in nude mice bearing human tumors. The results of the sensitivity study were well correlated with the clin. findings with the testing drugs. The survival rate of patients who received the drugs was higher than that of controls. The drugs used for testing were mitomycin C [50-07-7], 5-fluorouracil [51-21-8], and cyclophosphamide [50-18-0].

Answer 76:

Bibliographic Information

Positive interactions between interferon and chemotherapy due to direct tumor action rather than effects on host drug-metabolizing enzymes. Balkwill, F. R.; Mowshowitz, S.; Seilman, S. S.; Moodie, E. M.; Griffin, D. B.; Fantes, K. H.; Wolf, C. R. Imp. Cancer Res. Fund, London, UK. Cancer Research (1984), 44(11), 5249-55. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 102:4302 AN 1985:4302 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The mechanism of increased antitumor activity when human lymphoblastoid interferon [HuIFN-α(Ly)] and the drugs cyclophosphamide and Adriamycin are used in combination on a human tumor xenograft in nude mice has been investigated. HuIFN-α(Ly) did not affect hepatic levels of the drug-metabolizing enzymes cytochrome P450 or the glutathione S-transferases. In contrast, mouse interferon caused significant and differential changes in the isozymic forms of these enzymes. However, addn. of mouse interferon to the HuIFN-α(Ly)/cyclophosphamide or Adriamycin combinations had no effect on the final result, and did not increase the toxicity of the combination therapy. These data provide evidence that the increased activity of the combination therapy is due to effects on the tumor rather than on the host. Further studies showed significant perturbations in the tumor cell cycle after in vivo combination therapy. Cyclophosphamide caused an accumulation in G2 and the addn. of HuIFN-α(Ly), which alone caused little change in cycle distribution, delayed this G2 block and strongly increased the no. of cells in S phase. A similar, although less pronounced, effect was seen with HuIFN-α(Ly)/Adriamycin therapy. The increase in S phase seen in combined therapy may account for the synergy seen.

Answer 77:

Bibliographic Information

Increased cytotoxic effects of various anticancer drugs by α-interferon (HLBI) on human tumor xenografts in nude mice. Nosoh, Yoshihiro; Yoshinaka, Ken; Yamaguchi, Masahiro; Tani, Tadanori; Toge, Tetsuya; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Gan to Kagaku Ryoho (1984), 11(8), 1623-8. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 101:163319 AN 1984:563319 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of 7 anticancer agents in combination with interferon on gastric cancer and malignant melanoma of human transplanted s.c. in nude mice was studied. Of the 7 drugs, mitomycin C [50-07-7] and adriamycin [23214-92-8] showed the greatest inhibition of tumor growth in combination with interferon.

Answer 78:

Bibliographic Information

Childhood rhabdomyosarcoma xenografts: responses to DNA-interacting agents and agents used in current clinical therapy. Houghton, Janet A.; Cook, Ruby L.; Lutz, Pamela J.; Houghton, Peter J. Div. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, USA. European Journal of Cancer & Clinical Oncology (1984), 20(7), 955-60. CODEN: EJCODS ISSN: 0277-5379. Journal written in English. CAN 101:163109 AN 1984:563109 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A lab. model of childhood rhabdomyosarcoma (RMS) has been used to evaluate cytotoxic agents used in current clin. protocols, and DNA-reacting agents that have had either limited or no evaluation in this histiotype. Seven lines of RMS each derived from a different patient were grown as xenografts in immune-deprived mice, six of these being from specimens derived from previously untreated

patients. Of the conventional' agents, vincristine [57-22-7] was the most effective. Of the other agents evaluated [L-phenylalanine mustard (L-PAM) [148-82-3], cis-dichlorodiammineplatinum (cis-DDP) [15663-27-1], mitomycin C [50-07-7] and 5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide (DTIC) [4342-03-4]], L-PAM caused complete regressions in six of seven lines, including those resistant to cyclophosphamide [50-18-0]. DTIC had marked activity in five tumors, and mitomycin C in three lines. Cyclophosphamide was active in five tumors, although efficacy was less marked in two lines in comparison to DTIC and mitomycin C.

Answer 79:

Bibliographic Information

Effect of five antineoplastic agents on tumor xenografts with different growth rates. Mattern, Juergen; Wayss, Klaus; Volm, Manfred. Dep. Exp. Pathol., German Cancer Res. Cent., Heidelberg, Fed. Rep. Ger. JNCI, Journal of the National Cancer Institute (1984), 72(6), 1335-9. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 101:103754 AN 1984:503754 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of cyclophosphamide (Cy) [50-18-0], doxorubicin (Dx) [23214-92-8], cisplatin (DDP) [15663-27-1], melphalan (L-PAM) [148-82-3], and vincristine (VCR) [57-22-7] on various human and animal tumor lines with different growth rates, growing as xenografts in NMRI (nu/nu) mice, were studied. Two types of response were obsd.: For Cy and Dx, the response of the xenografts was neg. correlated with tumor vol. doubling time (TD), indicating that rapidly growing tumors were more sensitive to these drugs than were slowly growing tumors. For DDP, L-PAM, and VCR, the effects were pos. correlated with the TD, indicating that slowly growing tumors were more sensitive to these drugs than rapidly growing tumors. The data are discussed in relation to the effects of the drugs on proliferating and nonproliferating cells obtained with other cell lines.

Answer 80:

Bibliographic Information

Chemosensitivity of human gastrointestinal and breast cancer xenografts in nude mice and predictability to clinical response of anticancer agents. Fujita, M.; Fujita, F.; Taguchi, T. Dep. Oncol. Surg., Osaka Univ., Osaka, Japan. Editor(s): Sordat, Bernard. Immune-Defic. Anim., Int. Workshop Immune-Defic. Anim. Exp. Res., 4th (1984), Meeting Date 1982, 311-15. Publisher: Karger, Basel, Switz CODEN: 51ONAB Conference written in English. CAN 101:103450 AN 1984:503450 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effectiveness of 13 drugs against 14 lines of human gastrointestinal and breast cancers xenografted in nude mice was studied. Despite identical origins of organ and similarities in histol. types, degrees of differentiation, and growth rate, each line of cancer demonstrated different spectra of sensitivity to various agents. The effectiveness of various chemotherapeutic agents against human gastric cancer xenografts in nude mice was compared with the clin. effects of these drugs in clin. trials and phase II studies. The results indicated that the nude mouse-human cancer system would be useful in preclin. secondary screening.

Answer 81:

Bibliographic Information

Induced and inherent resistance to alkylating agents in human small-cell bronchial carcinoma xenografts. Berman, R.; Steel, G. G. Radiother. Res. Unit, Inst. Cancer Res., Sutton, UK. British Journal of Cancer (1984), 49(4), 431-6. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 100:203254 AN 1984:203254 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Inherent and induced resistance was investigated in human small-cell lung cancer xenografts. Specimens from patients were established in immune suppressed mice; the sensitivity of the xenografts to cyclophosphamide [50-18-0], MeCCNU [13909-09-6], and melphalan [148-82-3] was detd. Clin. chemosensitivity data were available in 2 cases and inherent differences in sensitivity were noted both in the xenografts and clin. Radioactively-labeled melphalan uptake studies were performed with these 2 xenografts. A no. of different strategies to induce resistance were explored. Only 1 method proved to be successful and in only 1 of the xenografts; this was with cyclophosphamide. The induced resistant line was characterized in terms of the time course of its prodn., the degree of induced resistance, the growth rate, the cross-resistance pattern and stability of the phenotype; the possibility of altered antigenicity was also examd.

Answer 82:

Bibliographic Information

Renal cell carcinoma - xenotransplantation into immuno-suppressed mice. Kopper, L.; Magyarosy, E.; Nagy, P.; Lapis, K.; Szamel, I.; Eckhardt, S.; Csata, S.; Wabrosch, G.; Repassy, D. 1st Inst. Pathol. Exp. Cancer Res., Semmelweis Med. Univ., Budapest, Hung. Oncology (1984), 41(1), 19-24. CODEN: ONCOBS ISSN: 0030-2414. Journal written in English. CAN 100:150726 AN 1984:150726 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Twenty one human renal cell carcinomas (RCC) were xenotransplanted into artificially immunosuppressed mice. Four tumors grew successfully retaining some characteristics of the primary tumors (according to morphol. and karyotype anal.), but losing metastatic capacity. One of the serially transplantable tumors (HT 40) with hyperdiploid cellular DNA content and estrogen receptor positivity failed to respond to the single maximally tolerated dose of several cytotoxic agents.

Answer 83:

Bibliographic Information

Positive interactions between human interferon and cyclophosphamide or adriamycin in a human tumor model system. Balkwill, F. R.; Moodie, E. M. Imp. Cancer Res. Fund, London, UK. Cancer Research (1984), 44(3), 904-8. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 100:119141 AN 1984:119141 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Human lymphoblastoid interferon strongly increased the antitumor activity of suboptimal doses of 2 commonly used anticancer drugs, cyclophosphamide and Adriamycin, on a human breast tumor xenograft growing in nude mice. A combination of human lymphoblastoid interferon with either of these agents caused regression and in some cases total disappearance of tumors at doses of drug and interferon that, used singly, were capable only of inhibiting tumor growth. The combined therapy also resulted in a greatly increased survival. Studies with interferon and cyclophosphamide indicated that the antitumor activity was greatest when the 2 agents were administered simultaneously rather than sequentially.

Answer 84:

Bibliographic Information

Chemotherapy of human yolk sac tumor heterotransplanted in nude mice. Sawada, Masumi; Matsui, Yoshiaki; Okudaira, Yoshio. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. JNCI, Journal of the National Cancer Institute (1983), 71(6),

1221-5. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 100:96258 AN 1984:96258 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The chemotherapeutic effects of cis-diamminedichloroplatinum [15663-27-1] plus vinblastine [865-21-4] plus bleomycin [11056-06-7] (PVB) on 3 human yolk sac tumors (YST-1, YST-2, and YST-3) of the ovary, which were heterotransplanted into BALB/c nude mice, were compared with the effects of vincristine+actinomycin D+cyclophosphamide (VAC), the combination currently favored for treatment of yolk sac tumors. Both PVB and VAC significantly reduced the tumor vol. of all the treated tumors. The mean wts. of tumors in animals treated with PVB or VAC were, in percent of the mean tumor wt. in untreated animals: 1.3 and 1.6 for YST-1, 2.5 and 3.3 for YST-2, and 5.5 and 2.7 for YST-3, resp. A strong correlation was noted between tumor vol. and α-fetoprotein level in the sera of mice bearing YST-1 or TST-2 tumors.

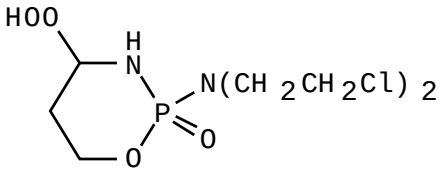
Answer 85:

Bibliographic Information

Antitumor effect and metabolic activation of cyclophosphamide and 4-hydroperoxycyclophosphamide in the human breast carcinoma (MX-1)-nude mouse system. Kubota, Tetsuro; Hanatani, Yuji; Tsuyuki, Ken; Nakada, Munehiko; Ishibiki, Kyuya; Abe, Osahiko; Kamataki, Tetsuya; Kato, Ryuichi. Sch. Med., Keio Univ., Tokyo, Japan. Gann (1983), 74(3), 437-44. CODEN: GANNA2 ISSN: 0016-450X. Journal written in English. CAN 99:63971 AN 1983:463971 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of cyclophosphamide (CPA) [50-18-0] and its active form, 4-hydroperoxy-CPA (I) [39800-16-3], against human breast carcinoma transplanted into nude mice (BALB/c nu/nu) were evaluated in terms of the decreases of hepatic drug-metabolizing enzymes in nude mice. A human breast carcinoma, MX-1, was implanted into the s.c. tissue of nude mice and a drug was administered i.v. once at 0.05, 0.1, or 0.15 mmol/kg, 1 or 3 wk after tumor inoculation. 4-Hydroperoxy-CPA was more effective than CPA as regards inhibition of tumor growth, and the difference in effect was greater when the drugs were administered 3 wk after tumor inoculation than 1 wk. The activity of CPA was depressed by a decrease of the hepatic drug-metabolizing enzymes which occurred as the tumor-bearing period increased. Therefore, the effects of masked derivs. of CPA may correlate with the changes in drug-metabolizing activities of tumor-bearing mice. The human tumor xenograft-nude mouse system is considered to be suitable for chemosensitivity tests with masked compds.



I

Answer 86:

Bibliographic Information

Chemotherapy and radiation therapy of human medulloblastoma in athymic nude mice. Friedman, Henry S.; Schold, S. Clifford, Jr.; Varia, Mahesh; Bigner, Darell D. Med. Cent., Duke Univ., Durham, NC, USA. Cancer Research (1983), 43(7), 3088-93. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 99:63962 AN 1983:463962 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The human medulloblastoma cell line TE-671 was grown s.c. and intracranially in athymic nude mice. Tumor-bearing animals treated with chemotherapeutic agents or radiation were compared to untreated tumor-bearing controls. Tumors growing s.c. were sensitive to cyclophosphamide [50-18-0] and vincristine [57-22-7] with growth delays in duplicate trials of 15.8/16.5 and 12.9/15.0 days, resp. These tumors were minimally responsive to the 2,5-bis(1-aziridinyl)-3,6-dioxodiethyl ester of 1,4-cyclohexadiene-1,4-dicarbamic acid [57998-68-2] and cis-diamminedichloroplatinum II [15663-27-1] and unresponsive to methotrexate [59-05-2], NSC 351521 [72732-56-0], NSC 409962 [154-93-8], and procarbazine [671-16-9]. Radiation therapy with 2500 or 1500 rads as a single fraction produced a marked response, with growth delays of 39.5 and 21.1 days, resp. Cyclophosphamide produced a significant increase in the median survival of mice with intracranial tumors. Vincristine produced a minimal increase in the median survival while no response was seen to the 2,5-bis(1-aziridinyl)-3,6-dioxodiethyl ester of 1,4-cyclohexadiene-1,4-dicarbamic acid at the dose level and schedule tested. This model system will allow further anal. of the therapeutic sensitivity of human medulloblastoma to other agents or combined-modality regimens.

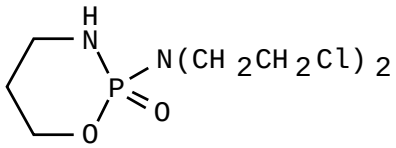
Answer 87:

Bibliographic Information

High dose cyclophosphamide treatment of human oat cell xenografts in immune deprived mice. Evans, B. D.; Smith, I. E.; Millar, J. L. R. Marsden Hosp., London, UK. British Journal of Cancer (1983), 47(2), 215-19. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 98:172706 AN 1983:172706 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Immunodeprived mice survived a high, otherwise LD of cyclophosphamide (I) [50-18-0] provided they had been "primed" with a low dose (50 mg/kg) of the drug 4 days earlier. These combinations were then tested on 2 oat cell xenograft lines (which are known to reproduce the chemotherapeutic responses of the parent tumors) grown in immunodeprived mice. In the treatment of the first oat cell xenograft, 200 mg/kg I produced a growth delay of 34 days in the unprimed group and 45 days in the primed group. At a dose of 300 mg/kg a growth delay could not be assessed in the control group as 16/17 of these unprimed mice bearing this xenograft died. However, 14/22 tumors went into complete remission in this group before death occurred. In contrast only 3/16 deaths occurred in the group of mice that were primed before receiving the same challenge dose. In these animals 19/26 tumors went into complete remission and were still completely absent when the expt. was terminated at 60 days. Using the second oat cell xenograft, 300 mg/kg I produced a growth delay of 27 days. However, at this dose level all the animals were dead by day 46. In mice which had been primed with 50 mg/kg I 4 days before the administration of 300 mg/kg a growth delay of 32 days was achieved and 2/9 animals were alive at day 60. Priming allows larger doses of I to be given to immunodeprived mice bearing human tumor xenografts than would normally be tolerated and priming does not alter the antitumor efficacy of the large challenge dose as measured by tumor growth delay or complete remission rate. As the tumors were human in origin it raises the question whether high dose cyclophosphamide therapy and priming have a role to play in the treatment of patients with oat cell carcinoma.



I

Answer 88:

Bibliographic Information

Effect of phase I and II chemotherapeutic agents against human lymphomas heterotransplanted in nude mice. Sordillo, Peter P.; Helson, Christiane; Lesser, Martin; Helson, Lawrence. Sch. Med., Cornell Univ., New York, NY, USA. Oncology (1983), 40(1), 15-17. CODEN: ONCOBS ISSN: 0030-2414. Journal written in English. CAN 98:154964 AN 1983:154964 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Ten chemotherapeutic agents, mostly phase I and II drugs, were tested for activity against 2 human lymphomas heterotransplanted in nude mice. Three of these agents have been tested in phase II trials in patients with lymphoma and found to lack activity; a corresponding lack of activity was found in lymphoma-bearing nude mice. Apart from cyclophosphamide [50-18-0], which is known to have activity against lymphoma and was used as a pos. control, only dianhydrogalactitol (DAG) [23261-20-3] had antitumor activity in the lymphoma-bearing nude mice. Tumor regressions induced by DAG in a heterotransplanted diffuse histiocytic lymphoma were significant.

Answer 89:

Bibliographic Information

New method for evaluating the effect of experimental chemotherapy on human xenografts in nude mice: use of lactate dehydrogenase isozyme. Hayata, Satoshi; Fujita, Masahide; Nakano, Yosuke; Kumagai, Michihiko; Hakozaki, Michinori; Taguchi, Tetsuo. Res. Inst. Microbial Dis., Osaka Univ., Osaka, Japan. Editor(s): Periti, Piero; Gialdroni Grassi, Giuliana. Curr. Chemother. Immunother., Proc. Int. Congr. Chemother., 12th (1982), Meeting Date 1981, 2 1283-4. Publisher: Am. Soc. Microbiol., Washington, D. C CODEN: 48HGAR Conference written in English. CAN 97:174303 AN 1982:574303 CAPLUS

Abstract

Monitoring human lactate dehydrogenase (I) [9001-60-9] isozyme 5 during chemotherapy in the nude mouse was more sensitive than conventional methods for evaluation of treatment. In H-55 (gastric) and H-62 (breast) tumors, good correlation between tumor vols. and human I were obsd. and the coeffs. were 0.686 and 0.803, resp. H-81 gastric cancer was very sensitive to TA-077 [70189-62-7] (100 mg/kg, weekly). S.c. tumor decreased after treatment and almost disappeared at the termination of the expt. Human I also decreased, and this decrease was greater than that obsd. for tumor size. The I isozyme method was more sensitive than the measurement of tumor size. In the ascitic tumor (Br-13 breast cancer) system, the effect of drugs was easily detd. by the human I level.

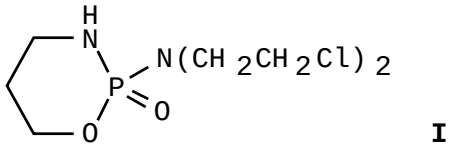
Answer 90:

Bibliographic Information

Pharmacokinetics of cyclophosphamide and cyclophosphamide metabolites in the mouse and their effect on the therapeutic effect of "activated" cyclophosphamide (4-hydroxycyclophosphamide). Voelcker, G.; Haeglsperger, R. Gustav-Embden-Zent. Biol. Chem., Johann Wolfgang Goethe-Univ., Frankfurt/Main, Fed. Rep. Ger. Arzneimittel-Forschung (1982), 32(6), 639-47. CODEN: ARZNAD ISSN: 0004-4172. Journal written in German. CAN 97:120024 AN 1982:520024 CAPLUS

Abstract

Following the i.v. injection of cyclophosphamide (I) [50-18-0] to nude mice with heterotransplanted human breast cancer 4-hydroxycyclophosphamide (II) [40277-05-2] was identified as the primary metabolite and phosphoramide mustard [10159-53-2] as a secondary metabolite. The cytotoxic effect of "activated I" (sum of II and aldophosphamide [35144-64-0]) was not proportional to the product of concn. and time (C x t) in blood; the cytotoxicity was greater with high blood concn. of activated I over a short period of time than with low concns. of activated I over a long period of time. Approx. 91% of 3H-labeled I was metabolized to its activated form (II plus aldophosphamide) and approx. 81% of this activated I was detoxified (first-pass effect) to 4-ketocyclophosphamide [27046-19-1] and carboxyphosphamide [22788-18-7]. The non-detoxified portion of activated I (approx. 10%) consisted of 80% II and 60% aldophosphamide.



I

Answer 91:

Bibliographic Information

Chemotherapy of human breast-carcinoma xenografts. Bailey, M. J.; Gazet, J. C.; Smith, I. E.; Steel, G. G. Inst. Cancer Res., Sutton/Surrey, UK. British Journal of Cancer (1980), 42(4), 530-6. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 94:95754 AN 1981:95754 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Sensitivities were varied for 5 lines of human breast carcinoma xenografts, grown and passaged in immune-suppressed mice, to cyclophosphamide [50-18-0], methotrexate [59-05-2], 5-fluorouracil [51-21-8], adriamycin [23214-92-8], vincristine [57-22-7], and melphalan [148-82-3], alone and in combination. The most effective single agent or combination differed for each tumor. This system may be useful for testing new cytotoxic agents and predicting clin. chemotherapy response.

Answer 92:

Bibliographic Information

Use of heterotransplants in diffusion chambers for determining the individual drug sensitivity of human ovarian cancer to chemotherapeutic drugs. Sobol, I. L.; Marenich, A. F. Cancer Res. Cent., Moscow, USSR. Byulleten Eksperimental'noi Biologii i Meditsiny (1979), 88(8), 243-5. CODEN: BEBMAE ISSN: 0365-9615. Journal written in Russian. CAN 91:150972 AN 1979:550972 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The sensitivity of 10 ovarian tumor heterotransplants in diffusion chambers in mice to hexamethylmelamine [645-05-6], cyclophosphane [50-18-0], 5-fluorouracil [51-21-8], methotrexate [59-05-2], dactinomycin [50-76-0], 17-hydroxyprogesterone caproate [630-56-8], and thiotepa [52-24-4] was variable. E.g., hexamethylmelamine, cyclophosphane, 5-fluorouracil, and methotrexate had a brief inhibiting effect in growth of a solid glandular cancer, inhibited growth of a glandular papillary cancer, and had no effect on growth of a papillary adenocarcinoma. In 4 of 5 cases where results of these expts. were compared with results of expts. obtained in the treatment of patients with the same drugs, exptl. results correlated with clin. findings.

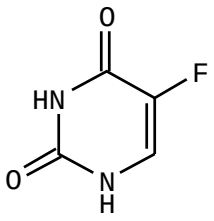
Answer 93:

Bibliographic Information

Chemotherapy of Nb rat adenocarcinoma of the prostate heterotransplanted into congenitally athymic (nude) mice: report of 5-fluorouracil and cyclophosphamide. Drago, Joseph R.; Maurer, Robert E.; Gershwin, M. Eric; Eckels, David D.; Goldman, Laurence B. Dep. Urol., Univ. California, Davis, CA, USA. Journal of Surgical Research (1979), 26(4), 400-3. CODEN: JSGRA2 ISSN: 0022-4804. Journal written in English. CAN 91:83171 AN 1979:483171 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

5-Fluorouracil (I) [51-21-8] (80 mg/kg) injected i.p. once into congenitally athymic (nude) mice bearing rat prostatic adenocarcinoma produced marked tumor regression. Cyclophosphamide (II) [50-18-0] (100 mg/kg/day) injected i.p. for 7 days into athymic mice with an autonomous tumor inhibited tumor growth but was not as effective as I.



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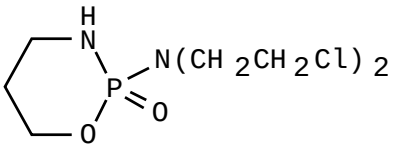

II

Answer 94:

Bibliographic Information

Phase II study: treatment of non-Hodgkin's lymphoma with an oral antitumor derivative of bis(2,6-dioxopiperazine). Ohno R; Yamada K; Hirano M; Shirakawa S; Tanaka M; Oguri T; Kodera Y; Mitomo Y; Ikeda Y; Yokomaku S; + Department of Medicine, Nagoya University School of Medicine, Branch Hospital, Japan Journal of the National Cancer Institute (1992), 84(6), 435-8. Journal code: 7503089. ISSN:0027-8874. (CLINICAL TRIAL); Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 1538420 AN 92167304 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

BACKGROUND: Although razoxane (ICRF-159), a derivative of bis(2,6-dioxopiperazine), has shown significant antitumor activity in several murine tumors, inadequate bioavailability has limited its clinical efficacy. Sobuzoxane (MST-16), another derivative of bis(2,6-dioxopiperazine), has shown activity against a broad spectrum of murine tumors and human tumor xenografts in nude mice and a lack of cross-resistance to vincristine, doxorubicin, cyclophosphamide, fluorouracil, etoposide, and mitomycin C. These findings suggest that MST-16 has a mode of cytocidal activity different from that of other antitumor agents. PURPOSE: The present late phase II study was conducted to evaluate the clinical efficacy and toxicity of MST-16 in non-Hodgkin's lymphoma (NHL). METHODS: As part of a multi-institutional cooperative study, we conducted a study of MST-16 in 27 patients with NHL who were assessable for drug efficacy and toxicity. MST-16, a bis(2,6-dioxopiperazine) analogue and an inhibitor of topoisomerase II, was administered orally at a dose of 1600 mg/m2 a day for 5-7 days at intervals of 2-3 weeks. RESULTS: Response consisted of one complete remission and seven partial remissions in 27 assessable patients. Response was achieved at a median of 13 days (range, 9-62 days) after initiation of therapy and lasted a median of 46 days (range, 29-155 days). Major toxic effects were leukopenia in 70% of the patients, thrombocytopenia in 44%, and gastrointestinal disorders in 37%. CONCLUSIONS: MST-16 was shown to be effective in NHL and deserves further clinical trial, since the drug shows little cross-resistance to available antitumor drugs. IMPLICATIONS: Phase II clinical studies of MST-16 in treatment of breast cancer, gastric cancer, and adult T-cell leukemia and lymphoma are also being conducted in Japan. Future trials of combination chemotherapy using MST-16 with other antitumor drugs are warranted in view of the additive effects observed in studies of MOLT-3 cells and studies of L1210 leukemia in mice.

Answer 95:

Bibliographic Information

Local adoptive immunotherapy of human head and neck cancer xenografts in nude mice with lymphokine-activated killer cells and interleukin 2. Sacchi M; Snyderman C H; Heo D S; Johnson J T; d'Amico F; Herberman R B; Whiteside T L Department of Otolaryngology, University of Pittsburgh School of Medicine, Pennsylvania 15261 Cancer research (1990), 50(10), 3113-8. Journal code: 2984705R. ISSN:0008-5472. Journal;

Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 2334906 AN 90242289 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The efficacy of local adoptive immunotherapy with human lymphokine-activated killer cells and recombinant interleukin 2 (rIL-2) in growth inhibition of established squamous cell carcinoma of the head and neck (SCCHN) was evaluated in a nude mouse model. The model of xenografted SCCHN was established by s.c. injections of in vitro maintained tumor cells (2-10 x 10(6) cells/mouse) into the flank of splenectomized animals pretreated with cyclophosphamide (200 mg/kg). The SCCHN line used was tumorigenic in 95% of the appropriately conditioned nude mice. Inhibition of tumor growth by locally administered effector cells was the end point of the study, since the tumors did not metastasize within 6 weeks of tumor challenge. Either i.p. or local administration of rIL-2 alone (1000 units/day) to the tumor site daily for 2 weeks resulted in a significant inhibition of tumor growth. In the absence of detectable natural killer activity in these mice, a modest dose of rIL-2 had a direct antitumor effect on SCCHN cells in vivo. In addition, complete inhibition of tumor growth was achieved with 3 times weekly injections of 5-10 x 10(6) lymphokine-activated killer cells delivered to the tumor site and 1000 units of rIL-2 administered locally every day for 2 weeks. Our data indicate that local or systemic immunotherapy with rIL-2 alone or local adoptive immunotherapy with an adequate dose of lymphokine-activated killer cells plus rIL-2 may be effective in preventing the growth of established SCCHN tumors in vivo.

Answer 96:

Bibliographic Information

Evidence of a role for NK cells in oxazaphosphorine-mediated tumor regression. Reissmann T; Hilgard P; Voegeli R; Zeller J ASTA Pharma AG, Department of Experimental Cancer Research, Bielefeld, Federal Republic of Germany Journal of cancer research and clinical oncology (1989), 115(6), 525-30. Journal code: 7902060. ISSN:0171-5216. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 2606928 AN 90110303 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The present studies showed that nude mice xenotransplanted with L5222 leukemia responded as did syngeneic BD IX rats to low doses of mafosfamide or cyclophosphamide. Unlike rats, nude mice rarely showed resistance to a second tumor challenge. The observation that concurrent treatment of rats with cyclosporin A did not alter the rate of survival clearly indicated a T-cell-independent mechanism of tumor defense. The incidence of lung colonies from i.v. injected Lewis lung-tumor cells could be enhanced by a high dose pretreatment with mafosfamide or cyclophosphamide, whereas pretreatment at low doses was inhibitory. Since identical experiments carried out in NK-cell-deficient C57Bl/6 "beige" mice did not show such an effect, NK cells appeared to represent a possible effector cell in oxazaphosphorine-mediated antitumor effects. This assumption was further supported by the fact that enhanced NK cell activity could be observed in the 51Cr release assay using spleen cells from mafosfamide-treated L5222-bearing rats. The transplantation of the unrelated syngeneic ovarian carcinoma OV-342 to animals that had previously been cured of L5222 leukemia did not lead to the rejection of this tumor. This indicates that a specific resistance against L5222 leukemia had developed. In contrast, a T-cell-dependent antitumor effect was demonstrated for mafosfamide in the MOPC-315 mouse plasmocytoma. Therefore, we conclude that the effector cell for tumor rejection depends on the type of tumor. This, of course, does not exclude a common target cell for the immunopharmacological activity of oxazaphosphorines.

Answer 97:

Bibliographic Information

Ineffective photodynamic therapy (PDT) in a poorly vascularized xenograft model. White L; Gomer C J; Doiron D R; Szirth B C Prince of Wales Children's Hospital, Randwick, Sydney, NSW, Australia British journal of cancer

(1988), 57(5), 455-8. Journal code: 0370635. ISSN:0007-0920. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 3395551 AN 88281355 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Haematoporphyrin derivative (HPD) photodynamic therapy (PDT) may have clinical application in the management of patients with retinoblastoma. Heterotransplantation of retinoblastoma cells into the anterior chamber of the nude mouse eye and the subsequent growth of small tumour masses has provided a model for evaluation of various therapeutic modalities. Ninety-four evaluable xenograft tumours in 54 nude mice were randomized to receive one of the following treatments: cyclophosphamide (CPM) alone, HPD-PDT alone, CPM followed by HPD-PDT, HPD-PDT followed by CPM, or saline control. Responses were demonstrated after CPM treatment in all three relevant groups. However, HPD-PDT was found to be ineffective either alone or as a contributor in the double modality treatment groups. The small tumour masses treated can be demonstrated histologically to be avascular. It is proposed that although the same retinoblastoma cells in different circumstances are responsive to HPD-PDT, no clinical response is demonstrable utilizing this model, due to the absence of tumor vascularity.

Answer 98:

Bibliographic Information

Subrenal capsule assay for chemosensitivity testing. Kusuyama T; Fujita M; Shimozuma K; Orikasa H; Usugane M; Taguchi T Gan to kagaku ryoho. Cancer & chemotherapy (1987), 14(4), 1143-9. Journal code: 7810034. ISSN:0385-0684. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 3105468 AN 87183601 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The subrenal capsule (SRC) assay for cancer chemotherapy was tested according to Bogden's methodology. Of 37 patients providing tumor tissue for assay, 29 cases were considered suitable for evaluable assays. Fourteen patients had clinically evaluable diseases and 10 cases were evaluable for SRC assays. Correspondence between sensitive assay and clinical sensitivity was seen in 2 cases, and that between resistant assay and clinical resistance was seen in 4 cases. Discordance between sensitive assay and clinical resistance was seen in 4 cases. In histological studies, cancer tissues implanted in the subrenal space in immunocompetent mice did not show marked proliferation and were replaced by prominent leukocyte infiltration and fibrosis on day 6 after inoculation. The degree of leukocyte infiltration in the xenografts in the mice administered some anti-cancer drugs was slight in comparison with that in untreated control mice, which showed a remarkable trend in xenografts treated with 5-fluorouracil and cyclophosphamide, respectively. Our study suggests that there are many problems involved in the SRC assay methodology of Bogden, and that careful examination of this aspect will be required.

Answer 99:

Bibliographic Information

The possibility of assaying Wistar rat bone marrow CFUs in a xenogeneic (rat-to-mouse) system. Fohlmeister I; Hohentanner O Natural immunity and cell growth regulation (1985), 4(4), 221-8. Journal code: 8407979. ISSN:0254-7600. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 2866442 AN 86065220 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The possibility of replacing the space-consuming rat-to-rat colony-forming unit (CFUs) assay by rat-to-mouse assay systems was examined using Wistar rat bone marrow. After considering the published results on the responsiveness of mouse strains to hemopoietic xenografts and on the ways to abrogate "xenogeneic resistance', we tested C57B1/6J and C3H/He mice conditioned by cyclophosphamide (CY) and/or whole-body irradiation in the following combinations: 850 rad C57Bl; 850 rad + CY C57Bl; 800 rad + CY C3H. A linear relationship between the number of cells injected and the macroscopical spleen colony count could be demonstrated with all three combinations. However, we observed a high number of endogenous colonies in the 850 rad C57B1 system. The results were confirmed by karyotype analysis. Colony yield and seeding efficiency with 800 rad + CY C3H were comparable to the rat-to-rat assay, but were considerably lower in the case of 850 rad + CY C57B1. In the latter system, the colonies were primarily erythroid.

Answer 100:

Bibliographic Information

Synthesis and preliminary antitumor evaluation of 4-(SR)-sulfido-cyclophosphamides. Peter G; Hohorst H J Cancer chemotherapy and pharmacology (1979), 3(3), 181-8. Journal code: 7806519. ISSN:0344-5704. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 527208 AN 80111504 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Crystalline 4-(SR)-sulfidocyclophosphamides, sulfido derivatives of activated cyclophosphamide (4-hydroxycyclophosphamide), were synthesized by ozonation of cyclophosphamide and reaction of the intermediate 4-hydroxycyclophosphamide with various thiols (HSR). The products were characterized by elemental analysis, 1H NMR and IR spectroscopy, and mass spectrometry. 1H NMR and polarimetric analysis demonstrated that they consist of racemic cis-isomers that are stable in the crystalline state at room temperature. In aqueous solution these derivatives are hydrolyzed to 4-hydroxycyclophosphamide and the corresponding thiol, with half-lives ranging between 4 and 17 min at 37 degrees C and pH 7. The cytotoxicity of 4-(S-ethyl)- and 4-(S-ethanol)-sulfidocyclophosphamide against Yoshida sarcoma ascites cells and the toxicity in rats were found to be practically identical with those of activated cyclophosphamide. A preliminary evaluation of the curative effect after a single IV injection of 4-(S-ethane)- and 4-(S-ethanol)-sulfidocyclophosphamide in rats bearing Yoshida ascites sarcoma or of 4-(S-ethanol)-sulfidocyclophosphamide in nu/nu mice bearing human breast carcinoma xenografts suggested that these sulfido derivatives possess the same oncostatic efficacy as activated cyclophosphamide itself.

Answer 101:

Bibliographic Information

Therapeutic effectivity of cyclophosphamide and cyclophosphamide metabolites against a human breast cancer heterotransplanted to nu/nu mice. Voelcker G; Bastert G; Fortmeyer H P; Haeglsperger R; Hiltl G; Peter G; Hohorst H J Archives of gynecology (1979), 228(1-4), 452-4. Journal code: 7901051. ISSN:0170-9925. Journal; Article; (JOURNAL ARTICLE) written in German. PubMed ID 485432 AN 80019117 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))